

Sublinear Time Motif Discovery from Multiple Sequences*

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Abstract

A natural probabilistic model for motif discovery has been used to experimentally test the quality of motif discovery programs. In this model, there are k background sequences, and each character in a background sequence is a random character from an alphabet Σ . A motif $G = g_1g_2 \dots g_m$ is a string of m characters. Each background sequence is implanted a probabilistically generated approximate copy of G . For a probabilistically generated approximate copy $b_1b_2 \dots b_m$ of G , every character b_i is probabilistically generated such that the probability for $b_i \neq g_i$ is at most α . We develop three algorithms that under the probabilistic model can find the implanted motif with high probability via a tradeoff between computational time and the probability of mutation. Each algorithm has the preprocessing part and the voting part. We use a pair of function $(t_1(n, k), t_2(n, k))$ to describe the computational complexity of motif detection algorithm, where n is the largest length of input sequence, and k is the number of sequences. Function $t_1(n, k)$ is the time complexity for the part for preprocessing and $t_2(n, k)$ is the time complexity for recovering one character for motif after preprocessing. The total time is $O(t_1(n, k) + t_2(n, k)|G|)$.

(1) There exists a randomized algorithm such that there are positive constants c_0 and c_1 that if the alphabet size is at least 4, the number of sequences is at least $c_1 \log n$, the motif length is at least $c_0 \log n$, and each character in motif region has probability at most $\frac{1}{(\log n)^{2+\mu}}$ of mutation for some fixed $\mu > 0$, then motif can be recovered in $(O(\frac{n}{\sqrt{h}}(\log n)^{\frac{7}{2}} + h^2 \log^2 n), O(\log n))$ time, where n is the longest length of any input sequences, and $h = \min(|G|, n^{\frac{2}{5}})$. The algorithm total time is sublinear if the motif length $|G|$ is in the range $[(\log n)^{7+\mu}, \frac{n}{(\log n)^{1+\mu}}]$. This is the first sublinear time algorithm with rigorous analysis in this model.

(2) There exists a randomized algorithm such that there are positive constants c_0, c_1 , and α that if the alphabet size is at least 4, the number of sequences is at least $c_1 \log n$, the motif length is at least $c_0 \log n$, and each character in motif region has probability at most α of mutation, then motif can be recovered in $(O(\frac{n^2}{|G|}(\log n)^{O(1)}), O(\log n))$ time.

(3) There exists a deterministic algorithm such that there are positive constants c_0, c_1 , and α that if the alphabet size is at least 4, the number of sequences is at least $c_1 \log n$, the motif length is at least $c_0 \log n$, and each character in motif region has probability at most α of mutation, then motif can be recovered in $(O(n^2(\log n)^{O(1)}), O(\log n))$ time.

The methods developed in this paper have been used in the software implementation. We observed some encouraging results that show improved performance for motif detection compared with other softwares.

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1. Introduction

Motif discovery is an important problem in computational biology and computer science. For instance, it has applications in coding theory [3, 6], locating binding sites and conserved regions in unaligned sequences [8, 12, 20, 21], genetic drug target identification [11], designing genetic probes [11], and universal PCR primer design [2, 11, 16, 19].

This paper focuses on the application of motif discovery to find conserved regions in a set of given DNA, RNA, or protein sequences. Such conserved regions may represent common biological functions or structures. Many performance measures have been proposed for motif discovery. Let C be a subset of 0-1 sequences of length n . The *covering radius* of C is the smallest integer r such that each vector in $\{0, 1\}^n$ is at a distance at most r from a string in C . The decision problem associated with the covering radius for a set of binary sequences is NP-complete [3]. The similar closest string and substring problems were proved to be NP-hard [3, 11]. Some approximation algorithms have been proposed. Li et al. [14] gave an approximation scheme for the closest string and substring problems. The related consensus patterns problem is that given n sequences s_1, \dots, s_n , find a region of length L in each s_i , and a string s of length L so that the total Hamming distance from s to these regions is minimized. Approximation algorithms for the consensus patterns problem were reported in [13]. Furthermore, a number of heuristics and programs have been developed [1, 9, 10, 18, 22].

In many applications, motifs are faint and may not be apparent when two sequences alone are compared but may become clearer when more sequences are compared together [7]. For this reason, it has been conjectured that comparing more sequences together can help with identifying faint motifs. This paper is a theoretical approach with a rigorous probabilistic analysis.

We study a natural probabilistic model for motif discovery. In this model, there are k background sequences and each character in the background sequence is a random character from an alphabet Σ . A motif $G = g_1g_2 \dots g_m$ is a string of m characters. Each background sequence is implanted a probabilistically generated approximate copy of G . For a probabilistically generated approximate copy $b_1b_2 \dots b_m$ of G , every character b_i is probabilistically generated such that the probability for $b_i \neq g_i$, which is called a *mutation*, is at most α . This model was first proposed in [18] and has been widely used in experimentally testing motif discovery programs [1, 9, 10, 22]. We note that a mutation in our model converts a character g_i in the motif into a different character b_i without probability restriction. This means that a character g_i in the motif may not become any character b_i in $\Sigma - \{g_i\}$ with equal probability.

We develop three algorithms that under the probabilistic model, one can find the implanted motif with high probability via a tradeoff between computational time and the probability of mutation. Each algorithm has the preprocessing phase and the voting phase. We use a pair of function $(t_1(n, k), t_2(n, k))$ to describe the computational complexity of motif detection algorithm, where n is the largest length of input sequence, and k is the number of sequences. Function $t_1(n, k)$ is the time complexity for the part for preprocessing, and $t_2(n, k)$ is the time complexity for recovering one character for motif after preprocessing. The total time is $O(t_1(n, k) + t_2(n, k)|G|)$.

(1) There exists a randomized algorithm such that there are positive constants c_0 and c_1 that if the alphabet size is at least 4, the number of sequences is at least $c_1 \log n$, the motif length is at least $c_0 \log n$, and each character in motif region has probability at most $\frac{1}{(\log n)^{2+\mu}}$ of mutation for some fixed $\mu > 0$, then motif can be recovered in $(O(\frac{n}{\sqrt{h}}(\log n)^{\frac{7}{2}} + h^2 \log^2 n), O(\log n))$ time, where n is the longest length of any input sequences, and $h = \min(|G|, n^{\frac{2}{5}})$. The algorithm total time is sublinear if the motif length $|G|$ is in the range $[(\log n)^{7+\mu}, \frac{n}{(\log n)^{1+\mu}}]$. This is the first sublinear time algorithm with rigorous analysis in this model.

(2) There exists a randomized algorithm such that there are positive constants c_0, c_1 , and α

that if the alphabet size is at least 4, the number of sequences is at least $c_1 \log n$, the motif length is at least $c_0 \log n$, and each character in motif region has probability at most α of mutation, then motif can be recovered in $(O(\frac{n^2}{|G|}(\log n)^{O(1)}), O(\log n))$ time.

(3) There exists a deterministic algorithm such that there are positive constants c_0, c_1 , and α that if the alphabet size is at least 4, the number of sequences is at least $c_1 \log n$, the motif length is at least $c_0 \log n$, and each character in motif region has probability at most α of mutation, then motif can be recovered in $(O(n^2(\log n)^{O(1)}), O(\log n))$ time.

The research in this model has been reported in [4, 5, 15]. In [4], Fu et al. developed an algorithm that needs the alphabet size to be a constant that is much larger than 4. In [5], our algorithm cannot handle all possible motif patterns. In [15], Liu et al. designed algorithm that runs in $O(n^3)$ time and is lack of rigorous analysis about its performance. The motif recovery in this natural and simple model has not been fully understood and seems a complicated problem.

This paper presents two new randomized algorithms and one new deterministic algorithm. They make advancements in the following aspects: 1. The algorithms are much faster than those before. Our algorithms can even run in sublinear time. 2. They can handle any motif pattern. 3. The restriction for the alphabet size is as small as four, giving them potential applications in practical problems since gene sequences have an alphabet size 4. 4. All algorithms have rigorous proofs about their performances.

The entire Recover-Motif is described in Section 4.2. We analyze Algorithm Recover-Motif in Section 5.

2. Notations and the Model of Sequence Generation

For a set A , $|A|$ denotes the number of elements in A . Σ is an alphabet with $|\Sigma| = t \geq 2$. For an integer $n \geq 0$, Σ^n is the set of sequences of length n with characters from Σ . For a sequence $S = a_1 a_2 \cdots a_n$, $S[i]$ denotes the character a_i , and $S[i, j]$ denotes the substring $a_i \cdots a_j$ for $1 \leq i \leq j \leq n$. $|S|$ denotes the length of the sequence S . We use \emptyset to represent the empty sequence, which has length 0.

Let $G = g_1 g_2 \cdots g_m$ be a fixed sequence of m characters. G is the motif to be discovered by our algorithm. A $\Theta_\alpha(n, G)$ -sequence has the form $S = a_1 \cdots a_{n_1} b_1 \cdots b_m a_{n_1+1} \cdots a_{n_2}$, where $n_2 + m \leq n$, each a_i has probability $\frac{1}{t}$ to be equal to π for each $\pi \in \Sigma$, and b_i has probability at most α not equal to g_i for $1 \leq i \leq m$, where $m = |G|$. $\aleph(S)$ denotes the motif region $b_1 \cdots b_m$ of S . A mutation converts a character g_i in the motif into an arbitrary different character b_i without probability restriction. This allows a character g_i in the motif to change into any character b_i in $\Sigma - \{g_i\}$ with even different probability. The motif region of S may start at an arbitrary or worst-case position in S . Also, a mutation may convert a character g_i in the motif into an arbitrary or worst-case different character b_i only subject to the restriction that g_i will mutate with probability at most α .

A $\Psi(n, G)$ -sequence has the form $S = a_1 \cdots a_{n_1} b_1 \cdots b_m a_{n_1+1} \cdots a_{n_2}$, where $n_2 + m \leq n$, each a_i has probability $\frac{1}{t}$ to be equal to π for each $\pi \in \Sigma$, and there are at most $O(1)$ characters b_i not equal to g_i for $1 \leq i \leq m$ and each mutation occurs at a random position of G , where $m = |G|$.

For two sequences $S_1 = a_1 \cdots a_m$ and $S_2 = b_1 \cdots b_m$ of the same length, let the *relative Hamming distance* $\text{diff}(S_1, S_2) = \frac{|\{i | a_i \neq b_i (i=1, \dots, m)\}|}{m}$.

Definition 1. For two intervals $[i_1, j_1]$ and $[i_2, j_2]$, define $\text{shift}([i_1, j_1], [i_2, j_2]) = \min(|i_1 - i_2|, |j_1 - j_2|)$.

3. Brief Introduction to Algorithm

Every detection algorithm in this paper has two phases. The first phase is preprocessing so that the motif regions from multiple sequences can be aligned in the same column region. The second phase is to recover the motif via voting. We use a pair of function $(t_1(n, k), t_2(n, k))$ to describe the computational complexity of motif detection algorithm. Function $t_1(n, k)$ is the time complexity for the preprocessing phase and $t_2(n, k)$ is the time complexity for outputting one character for motif in the voting phase.

The motif G is a pattern unknown to algorithm Recover-Motif, and algorithm Recover-Motif will attempt to recover G from a series of $\Theta(n, G, \alpha)$ -sequences generated by the probabilistic model.

3.1. Algorithm

The algorithm first detects a position that is close to the left motif boundary in a sequence. It finds such a position via sampling and collision between two sequences. After the rough left boundary a sequence is found, it is used to find the rough boundaries of the rest of the sequences. Similarly, we find those right boundaries of motif among the input sequences. The exact left boundary of each motif region will be detected in the next phase via voting. Each character of the motif is recovered by voting among all the characters at the same positions in the motif regions of input sequences.

Descriptions of Algorithm

Input: $Z = Z_1 \cup Z_2$, where $Z_1 = \{S'_1, \dots, S'_{2k_1}\}$ and $Z_2 = \{S''_1, \dots, S''_{k_2}\}$ are two sets of input sequences.

Output: Planted motif in each sequence and consensus string

Start:

Randomly select sample points from each sequence both in Z_1 and Z_2

For each pair of sequences selected from Z_1 and Z_2 ,

Find the rough left and rough right boundaries.

Improve rough boundaries.

If motif boundaries of each sequence in Z_2 are not empty,

Use Voting algorithm to get the planted motifs.

End of Algorithm

3.2. An Example

We provide the following example for the brief idea of our algorithm. Let the following input strings be defined as below. We assume that the original motif is **TTTTTAACGATTAGCS**. The motif part is displayed with bold font, and the mutation characters in the motif region are displayed with small font.

3.2.1. Input Sequences

It contains two groups $Z_1 = \{S'_1, S'_2\}$ and $Z_2 = \{S''_1, S''_2, S''_3, S''_4, S''_5\}$.

$Z_1 :$

$S'_1 = GTACCATGGATTATTAACGATTAGCSTAGAGGACCTA.$

$S'_2 = AATCCTTACTTTTAACGATTAGCSGTC.$

The above two strings are used to detect the initial motif region and use them to deal with the motif in the second group below.

Z_2 :

$$\begin{aligned} S_1'' &= ATTCGATCCAGTTTTTAACGGTTAGCSCAATTACTTAG. \\ S_2'' &= GCATTGCATTTTTTAACGATTACCSGTACTTAGCTAGATC. \\ S_3'' &= TCAGGGCATCGAGACTTTTTTAGCGATTAGCSCTAGAATCAGACCT. \\ S_4'' &= GTACCTGGCATTGAACGTTTTTAACGATTAGCATGCAGATGGACCTTTA. \\ S_5'' &= AATGGATCAGATTTTTTAACGATTTCGCSCTAGATTCAG. \end{aligned}$$

3.2.2. Select Sample Points

Some sample points of two sequences in Z_1 are selected and marked.

$$\begin{aligned} S_1' &= GT\dot{A}CC\dot{A}TG\dot{G}AT\dot{T}ATTA\dot{A}CGA\dot{T}T\dot{A}GC\dot{S}TAG\dot{A}G\dot{G}ACCT\dot{A}. \\ S_2' &= \dot{A}AT\dot{C}CTT\dot{A}C\dot{T}TTTT\dot{A}AC\dot{G}A\dot{T}TA\dot{G}CS\dot{G}TC. \end{aligned}$$

3.2.3. Collision Detection

In this step, the left and right rough boundaries of two sequences will be marked. The following show the left collision, which happens nearby the left motif boundary and are marked by two overline \overline{TATT} and \overline{TTTT} subsequences.

$$\begin{aligned} S_1' &= GT\dot{A}CC\dot{A}TG\dot{G}AT\overline{\dot{T}ATTA}\dot{A}CGA\dot{T}T\dot{A}GC\dot{S}TAG\dot{A}G\dot{G}ACCT\dot{A}. \\ S_2' &= \dot{A}AT\dot{C}CTT\dot{A}C\overline{\dot{T}TTTT}\dot{A}AC\dot{G}A\dot{T}TA\dot{G}CS\dot{G}TC. \end{aligned}$$

The following show the right collision, which happens nearby the right motif boundary and are marked by two overline \overline{TTAG} subsequences.

$$\begin{aligned} S_1' &= GT\dot{A}CC\dot{A}TG\dot{G}AT\dot{T}ATTA\dot{A}CGA\dot{T}\overline{\dot{T}AGC}\dot{S}TAG\dot{A}G\dot{G}ACCT\dot{A}. \\ S_2' &= \dot{A}AT\dot{C}CTT\dot{A}C\dot{T}TTTT\dot{A}AC\dot{G}A\dot{T}\overline{\dot{T}AGC}\dot{S}GTC. \end{aligned}$$

3.2.4. Improving the Boundaries

In the early phase of the algorithm, we first detect a small piece of motif in S_1' by comparing S_1' and S_2' . Assume “TATT” and “TTAG” are found in the left and right motif region of S_1' respectively. The rough motif length will be calculated via the difference of the location first character ‘T’ of the first subsequence and the location of the last character ‘G’ of the second subsequence. The position marked by “A” is the rough left boundary of motif and the position marked by “T” is the rough right boundary of motif in S_1' below.

$$\begin{aligned} S_1' &= GTACCATGG\dot{A}\underline{\dot{T}}TATTAACGATTAGCS\underline{\dot{T}}AGAGGACCTA. \\ S_2' &= AATCCTT\underline{\dot{A}}C\dot{T}TTTTAACGATTAGCS\underline{\dot{G}}TC. \end{aligned}$$

3.2.5. Select Sample Points for the Sequences in Z_2

Some sample points near the motif boundaries of S_1' are selected.

$$S_1'' = GTACCATGGAT\dot{T}A\dot{T}TAACGATT\dot{A}G\dot{C}STAGAGGACCTA.$$

Sample points are selected in each sequence in Z_2 .

$$\begin{aligned}
S_1'' &= A\dot{T}T\dot{C}\dot{G}A\dot{T}C\dot{C}\dot{A}\dot{G}T\dot{T}\dot{T}\dot{T}T\dot{A}A\dot{C}\dot{G}\dot{G}T\dot{T}A\dot{G}\dot{C}\dot{S}\dot{C}\dot{A}\dot{A}T\dot{T}A\dot{C}T\dot{T}\dot{A}\dot{G}. \\
S_2'' &= G\dot{C}A\dot{T}T\dot{G}\dot{C}A\dot{T}T\dot{T}\dot{T}\dot{T}T\dot{A}A\dot{C}\dot{G}A\dot{T}T\dot{A}\dot{C}\dot{C}\dot{S}\dot{G}T\dot{A}\dot{C}T\dot{T}\dot{A}\dot{G}\dot{C}T\dot{A}\dot{G}A\dot{T}\dot{C}. \\
S_3'' &= \dot{T}C\dot{A}\dot{G}\dot{G}\dot{G}C\dot{A}\dot{T}\dot{C}\dot{G}\dot{A}\dot{G}A\dot{C}T\dot{T}\dot{T}\dot{T}\dot{T}A\dot{G}\dot{C}\dot{G}A\dot{T}T\dot{A}\dot{G}\dot{C}\dot{S}\dot{C}T\dot{A}\dot{G}\dot{A}\dot{A}T\dot{C}\dot{A}\dot{G}\dot{A}\dot{C}\dot{T}. \\
S_4'' &= G\dot{T}\dot{A}\dot{C}\dot{C}T\dot{G}\dot{G}C\dot{A}\dot{T}\dot{T}\dot{G}\dot{A}\dot{A}\dot{C}\dot{G}T\dot{T}\dot{T}\dot{T}T\dot{A}A\dot{C}\dot{G}A\dot{T}T\dot{A}\dot{G}\dot{C}\dot{A}\dot{T}\dot{G}\dot{C}\dot{A}\dot{G}\dot{A}\dot{T}\dot{G}\dot{G}\dot{A}\dot{C}\dot{C}T\dot{T}\dot{T}\dot{A}. \\
S_5'' &= A\dot{A}\dot{T}\dot{G}\dot{G}\dot{A}\dot{T}\dot{C}\dot{A}\dot{G}\dot{A}\dot{T}\dot{T}\dot{T}\dot{T}T\dot{A}A\dot{C}\dot{G}A\dot{T}T\dot{C}\dot{G}\dot{C}\dot{S}\dot{C}T\dot{A}\dot{G}\dot{A}\dot{T}\dot{T}\dot{C}\dot{A}\dot{G}.
\end{aligned}$$

3.2.6. Collision Detection Between S_1' with the Sequences in Z_2

Some sample points near the motif boundaries of S_1' are selected.

$$S_1'' = GTACCATGGAT\dot{T}\dot{A}\dot{T}\dot{T}AACGATT\dot{A}\dot{G}\dot{C}\dot{S}\dot{T}\dot{A}\dot{G}\dot{A}\dot{G}\dot{G}\dot{A}\dot{C}\dot{C}\dot{T}\dot{A}.$$

Sample points are selected in each sequence in Z_2 .

$$\begin{aligned}
S_1'' &= A\dot{T}T\dot{C}\dot{G}A\dot{T}C\dot{C}\dot{A}\dot{G}T\dot{T}\dot{T}\dot{T}T\dot{A}A\dot{C}\dot{G}\dot{G}T\dot{T}A\dot{G}\dot{C}\dot{S}\dot{C}\dot{A}\dot{A}T\dot{T}A\dot{C}T\dot{T}\dot{A}\dot{G}. \\
S_2'' &= G\dot{C}A\dot{T}T\dot{G}\dot{C}A\dot{T}T\dot{T}\dot{T}\dot{T}T\dot{A}A\dot{C}\dot{G}A\dot{T}T\dot{A}\dot{C}\dot{C}\dot{S}\dot{G}T\dot{A}\dot{C}T\dot{T}\dot{A}\dot{G}\dot{C}T\dot{A}\dot{G}A\dot{T}\dot{C}. \\
S_3'' &= \dot{T}C\dot{A}\dot{G}\dot{G}\dot{G}C\dot{A}\dot{T}\dot{C}\dot{G}\dot{A}\dot{G}A\dot{C}T\dot{T}\dot{T}\dot{T}\dot{T}A\dot{G}\dot{C}\dot{G}A\dot{T}T\dot{A}\dot{G}\dot{C}\dot{S}\dot{C}T\dot{A}\dot{G}\dot{A}\dot{A}T\dot{C}\dot{A}\dot{G}\dot{A}\dot{C}\dot{T}. \\
S_4'' &= G\dot{T}\dot{A}\dot{C}\dot{C}T\dot{G}\dot{G}C\dot{A}\dot{T}\dot{T}\dot{G}\dot{A}\dot{A}\dot{C}\dot{G}T\dot{T}\dot{T}\dot{T}T\dot{A}A\dot{C}\dot{G}A\dot{T}T\dot{A}\dot{G}\dot{C}\dot{A}\dot{T}\dot{G}\dot{C}\dot{A}\dot{G}\dot{A}\dot{T}\dot{G}\dot{G}\dot{A}\dot{C}\dot{C}T\dot{T}\dot{T}\dot{A}. \\
S_5'' &= A\dot{A}\dot{T}\dot{G}\dot{G}\dot{A}\dot{T}\dot{C}\dot{A}\dot{G}\dot{A}\dot{T}\dot{T}\dot{T}\dot{T}T\dot{A}A\dot{C}\dot{G}A\dot{T}T\dot{C}\dot{G}\dot{C}\dot{S}\dot{C}T\dot{A}\dot{G}\dot{A}\dot{T}\dot{T}\dot{C}\dot{A}\dot{G}.
\end{aligned}$$

3.2.7. Improving the Motif Boundaries for the Sequences in Z_2

After the collision with the sequences in Z_2 , we obtain the rough location of motifs of the sequences in Z_2 . Their motif boundaries for the sequences in Z_2 are improved.

$$S_1'' = GTACCATGGAT\dot{T}\dot{A}\dot{T}\dot{T}AACGATT\dot{A}\dot{G}\dot{C}\dot{S}\dot{T}\dot{A}\dot{G}\dot{A}\dot{G}\dot{G}\dot{A}\dot{C}\dot{C}\dot{T}\dot{A}.$$

The improved motif boundaries of the sequences in Z_2 are marked below.

$$\begin{aligned}
S_1'' &= ATTCGATCCAG\dot{T}\dot{T}\dot{T}\dot{T}T\dot{A}A\dot{C}\dot{G}\dot{G}T\dot{T}A\dot{G}\dot{C}\dot{S}\dot{C}\dot{A}\dot{A}T\dot{T}A\dot{C}T\dot{T}\dot{A}\dot{G}. \\
S_2'' &= GCATTGC\dot{A}\dot{T}\dot{T}\dot{T}\dot{T}T\dot{A}A\dot{C}\dot{G}A\dot{T}T\dot{A}\dot{C}\dot{C}\dot{S}\dot{G}T\dot{A}\dot{C}T\dot{T}\dot{A}\dot{G}\dot{C}T\dot{A}\dot{G}\dot{A}\dot{T}\dot{C}. \\
S_3'' &= TCAGGGCATCGAG\dot{A}\dot{C}\dot{T}\dot{T}\dot{T}\dot{T}T\dot{A}\dot{G}\dot{C}\dot{G}A\dot{T}T\dot{A}\dot{G}\dot{C}\dot{S}\dot{C}T\dot{A}\dot{G}\dot{A}\dot{A}T\dot{C}\dot{A}\dot{G}\dot{A}\dot{C}\dot{T}. \\
S_4'' &= GTACCTGGCATTGAAC\dot{G}\dot{T}\dot{T}\dot{T}\dot{T}T\dot{A}A\dot{C}\dot{G}A\dot{T}T\dot{A}\dot{G}\dot{C}\dot{A}\dot{T}\dot{G}\dot{C}\dot{A}\dot{G}\dot{A}\dot{T}\dot{G}\dot{G}\dot{A}\dot{C}\dot{C}T\dot{T}\dot{T}\dot{A}. \\
S_5'' &= AATGGATCAG\dot{A}\dot{T}\dot{T}\dot{T}\dot{T}T\dot{A}A\dot{C}\dot{G}A\dot{T}T\dot{C}\dot{G}\dot{C}\dot{S}\dot{C}\dot{T}\dot{A}\dot{G}\dot{A}\dot{T}\dot{T}\dot{C}\dot{A}\dot{G}.
\end{aligned}$$

3.2.8. Motif Boundaries for the Sequences in Z_2

$$S_1'' = GTACCATGGAT\dot{T}\dot{A}\dot{T}\dot{T}AACGATT\dot{A}\dot{G}\dot{C}\dot{S}\dot{T}\dot{A}\dot{G}\dot{A}\dot{G}\dot{G}\dot{A}\dot{C}\dot{C}\dot{T}\dot{A}.$$

Use the pair (G_L, G_R) with $G_L = \dot{T}\dot{T}\dot{A}\dot{T}$ and $G_R = \dot{A}\dot{G}\dot{C}\dot{S}$ to find the motif boundaries in the sequences of Z_2 . The rough boundaries of the second group is marked below with underlines.

$$\begin{aligned}
S_1'' &= ATTCGATCCAG\dot{T}\dot{T}\dot{T}\dot{T}T\dot{A}A\dot{C}\dot{G}\dot{G}T\dot{T}A\dot{G}\dot{C}\dot{S}\dot{C}\dot{A}\dot{A}T\dot{T}A\dot{C}T\dot{T}\dot{A}\dot{G}. \\
S_2'' &= GCATTGC\dot{A}\dot{T}\dot{T}\dot{T}\dot{T}T\dot{A}A\dot{C}\dot{G}A\dot{T}T\dot{A}\dot{C}\dot{C}\dot{S}\dot{G}T\dot{A}\dot{C}T\dot{T}\dot{A}\dot{G}\dot{C}T\dot{A}\dot{G}\dot{A}\dot{T}\dot{C}. \\
S_3'' &= TCAGGGCATCGAG\dot{A}\dot{C}\dot{T}\dot{T}\dot{T}\dot{T}T\dot{A}\dot{G}\dot{C}\dot{G}A\dot{T}T\dot{A}\dot{G}\dot{C}\dot{S}\dot{C}T\dot{A}\dot{G}\dot{A}\dot{A}T\dot{C}\dot{A}\dot{G}\dot{A}\dot{C}\dot{T}. \\
S_4'' &= GTACCTGGCATTGAAC\dot{G}\dot{T}\dot{T}\dot{T}\dot{T}T\dot{A}A\dot{C}\dot{G}A\dot{T}T\dot{A}\dot{G}\dot{C}\dot{A}\dot{T}\dot{G}\dot{C}\dot{A}\dot{G}\dot{A}\dot{T}\dot{G}\dot{G}\dot{A}\dot{C}\dot{C}T\dot{T}\dot{T}\dot{A}. \\
S_5'' &= AATGGATCAG\dot{A}\dot{T}\dot{T}\dot{T}\dot{T}T\dot{A}A\dot{C}\dot{G}A\dot{T}T\dot{C}\dot{G}\dot{C}\dot{S}\dot{C}\dot{T}\dot{A}\dot{G}\dot{A}\dot{T}\dot{T}\dot{C}\dot{A}\dot{G}.
\end{aligned}$$

3.2.9. Extracting the Motif Regions

The motif regions of the second group will be extracted. The original motif is recovered via voting at each column.

$$\begin{aligned} G_1'' &= \text{TTTTTAACGGTTAGCS} \\ G_2'' &= \text{TTTTTAACGATTACCS} \\ G_3'' &= \text{TTTTTAGCGATTAGCS} \\ G_4'' &= \text{TTTTTAACGATTAGCA} \\ G_5'' &= \text{TTTTTAACGATTGCS} \end{aligned}$$

3.2.10. Recovering Motif via Voting

The original motif **TTTTTAACGATTAGCS** is recovered via voting at all columns. For example, the last **S** in the motif is recovered via voting among the characters **S**, **S**, **S**, **A**, **S** in the last column.

3.3. Our Results

We give an algorithm for the case with at most $\frac{1}{(\log n)^{2+\mu}}$ mutation rate. The performance of the algorithm is stated in Theorem 2. Theorem 2 implies Corollary 3 by selecting $k = c_1 \log n$ with some constant c_1 large enough.

Theorem 2. *Assume that μ is a fixed number in $(0, 1)$ and the alphabet size t is at least 4. There exists a randomized algorithm such that there is a constant c_0 that if the length of the motif G is at least $c_0 \log n$, then given k independent $\Theta(n, G, \frac{1}{(\log n)^{2+\mu}})$ -sequences, the algorithm outputs G' such that*

- 1) *with probability at most $e^{-\Omega(k)}$, $|G'| \neq |G|$, and*
 - 2) *for each $1 \leq i \leq |G|$, with probability at most $e^{-\Omega(k)}$, $G'[i] \neq G[i]$, and*
 - 3) *with probability at most $\frac{k}{n^3}$, the algorithm Recover-Motif does not stop in $(O(k(\frac{n}{\sqrt{h}}(\log n)^{\frac{5}{2}} + h^2 \log n)), O(k))$ time,*
- where n is the longest length of any input sequences, and $h = \min(|G|, n^{\frac{2}{5}})$.*

Corollary 3. *There exists a randomized algorithm such that there are positive constants c_0, c_1 and μ that if the alphabet size is at least 4, the number of sequences is at least $c_1 \log n$, the motif length is at least $c_0 \log n$, and each character in motif region has probability at most $\frac{1}{(\log n)^{2+\mu}}$ of mutation, then motif can be recovered in $(O(\frac{n}{\sqrt{h}}(\log n)^{\frac{7}{2}} + h^2 \log^2 n), O(\log n))$ time, where n is the longest length of any input sequences, and $h = \min(|G|, n^{\frac{2}{5}})$.*

We give a randomized algorithm for the case with $\Omega(1)$ mutation rate. The performance of the algorithm is stated in Theorem 4. Theorem 4 implies Corollary 5 by selecting $k = c_1 \log n$ with some constant c_1 large enough..

Theorem 4. *Assume that the alphabet size t is at least 4. There exists a randomized algorithm such that there is a constant c_0 that if the length of the motif G is at least $c_0 \log n$, then given k independent $\Theta(n, G, \mu)$ -sequences, the algorithm outputs G' such that*

- 1) *with probability at most $e^{-\Omega(k)}$, $|G'| \neq |G|$, and*
- 2) *for each $1 \leq i \leq |G|$, with probability at most $e^{-\Omega(k)}$, $G'[i] \neq G[i]$,*

3) with probability at most $\frac{k}{n^3}$, the algorithm Recover-Motif does not stop in $(O(k(\frac{n^2}{|G|}(\log n)^{O(1)} + h^2)), O(k))$,

where n is the longest length of any input sequences, and $h = \min(|G|, n^{\frac{2}{5}})$.

Corollary 5. *There exists a randomized algorithm such that there are positive constants c_0, c_1 , and α that if the alphabet size is at least 4, the number of sequences is at least $c_1 \log n$, the motif length is at least $c_0 \log n$, and each character in motif region has probability at most α of mutation, then motif can be recovered in $(O(\frac{n^2}{|G|}(\log n)^{O(1)}), O(\log n))$ time.*

We give a deterministic algorithm for the case with $\Omega(1)$ mutation rate. The performance of the algorithm is stated in Theorem 6. Theorem 6 implies Corollary 7 by selecting $k = c_1 \log n$ with some constant c_1 large enough.

Theorem 6. *Assume that the alphabet size t is at least 4. There exists a deterministic algorithm such that there is a constant c_0 that if the length of the motif G is at least $c_0 \log n$, then given k independent $\Theta(n, G, \mu)$ -sequences, algorithm runs in $(O(n^2(\log n)^{O(1)} + h^2k), O(k))$, and outputs G' such that*

- 1) with probability at most $e^{-\Omega(k)}$, $|G'| \neq |G|$, and
- 2) for each $1 \leq i \leq |G|$, with probability at most $e^{-\Omega(k)}$, $G'[i] \neq G[i]$,
- 3) with probability at most $\frac{k}{n^3}$, the algorithm Recover-Motif does not stop in $(O(k(n^2(\log n)^{O(1)} + h^2)), O(k))$ time,

where n is the longest length of any input sequences, and $h = \min(|G|, n^{\frac{2}{5}})$.

Corollary 7. *There exists a deterministic algorithm such that there are positive constants c_0, c_1 , and α that if the alphabet size is at least 4, the number of sequences is at least $c_1 \log n$, the motif length is at least $c_0 \log n$, and each character in motif region has probability at most α of mutation, then motif can be recovered in $(O(n^2(\log n)^{O(1)}), O(\log n))$ time.*

4. Algorithm Recover-Motif

In this section, we give an unified approach to describe three algorithms. The performance of the algorithms is stated in the Theorems 2, 4, and 6. The description of Algorithm Recover-Motif is given at section 4.2. The analysis of the algorithm is given at section 5.

4.1. Some Parameters

Definition 8.

- i. Constant x is selected to be 10. This parameter controls the failure probability of our algorithms to be at most $\frac{1}{2^x}$.
- ii. The size of alphabet is t that is at least 4.
- iii. Select a constant $\rho_0 \in (0, 1)$ to have inequality (1)

$$\rho_0 < \frac{t-1}{2t}. \tag{1}$$

iv. The constant $\epsilon \in (0, 1)$ is selected to satisfy

$$\epsilon < \min\left(\left(\frac{t-1}{t} - (2\rho_0 + 2\epsilon)\right), \frac{1}{5}\left(1 - \frac{2}{t-1} - \frac{4}{2^x}\right), \frac{1}{3}\right). \quad (2)$$

The existence of ϵ follows from inequality (1). The constant ϵ is used to control the mutation in the motif area. It is a part of parameter β defined in item (xiv) of this definition.

v. Let $c = e^{-\frac{\epsilon^2}{3}}$. The constant c is used to simply probabilistic bounds which are derived from the applications of Chernoff bounds (See Corollary 17).

vi. Define $r(y) = (\frac{1}{t-1} + \frac{c^y}{1-c})$.

vii. Define u_1 to be a large constant that for all $v \geq 0$,

$$\frac{2(v + u_1)c^{v+u_1}}{(1-c)^2} \leq \frac{1}{5 \cdot 2^x}. \quad (3)$$

viii. Select constant $\rho_1 \in (0, 1)$ such that

$$\frac{2}{t-1} + \frac{4}{2^x} + 5\epsilon + \rho_1 < 1. \quad (4)$$

The existence of ρ_1 follows from $\epsilon < \frac{1}{5}(1 - \frac{2}{t-1} - \frac{4}{2^x})$, which is implied by inequality (2).

ix. Select constant $\rho_2 \in (0, 1)$ and constant positive integer v large enough such that

$$\frac{6(v + u_1)c^v}{1-c} + \rho_2 < \rho_1, \quad \text{and} \quad (5)$$

$$\left(\frac{1}{2^x} + (v + u_1)\frac{c^v}{1-c} + \frac{c^v}{1-c} + \frac{1}{5 \cdot 2^x}\right) \leq 1/2. \quad (6)$$

x. Define $\varsigma_0 = \frac{1}{2^x}$, and $\varphi(v) = (v + u_1)(\frac{c^v}{1-c} + \frac{c^v}{1-c})$.

xi. Select constant α_0 such that

$$4(v-1)\alpha_0 + \alpha_0 < \rho_2, \quad \text{and} \quad (7)$$

$$\alpha_0 < \rho_0. \quad (8)$$

Adding inequalities (4), (5), and (7), we have inequality (9)

$$\left(\frac{2}{t-1} + \frac{4}{2^x} + 5\epsilon\right) + \frac{6(v + u_1)c^v}{1-c} + (4(v-1)\alpha_0 + \alpha_0) < 1. \quad (9)$$

By arranging the terms in inequality (9) and the definitions of $r(v)$ and $\varphi(v)$, we have inequality (10)

$$2\left((2(v-1)\alpha_0 + \frac{c^v}{1-c}) + r(v) + 2(\varsigma_0 + \varphi(v)) + 2\epsilon\right) + (\alpha_0 + \epsilon) < 1. \quad (10)$$

xii. The maximal mutation rate α for the second algorithm (Theorem 4) and third algorithm (Theorem 6) are selected as α_0 . Since the mutation rate of our sublinear time algorithm is bounded by $\frac{1}{(\log n)^{2+\mu}}$, the maximal mutation rate α for the first algorithm (Theorem 2) is less than α_0 when n is large enough. We always assume that all mutation rates α in our three algorithms are in the range $(0, \alpha_0]$.

xiii. Define $q(y) = 2(v-1)\alpha + \frac{2c^y}{1-c}$. By inequality (10), the definition of $q(y)$, and the fact $\alpha \in (0, \alpha_0)$, we have

$$2(q(v) + r(v) + 2(\varsigma_0 + \varphi(v)) + 2\epsilon) + (\alpha_0 + \epsilon) < 1. \quad (11)$$

Inequality (11) implies $q(v) \leq \frac{1}{2}$. By inequality (6), we have that

$$\left(\frac{1}{2^x} + (v + u_1)\frac{c^v}{1-c} + \frac{c^v}{1-c} + \frac{1}{5 \cdot 2^x}\right) + q(v) \leq 3/4 \quad (12)$$

xiv. Let $\beta = 2\alpha + 2\epsilon$. The parameter β controls the similarity of $\aleph(S)$ and the original motif G (see Lemma 26).

xv. Define $R = r(v)$.

xvi. We define the following Q_0 .

$$Q_0 = q(v). \quad (13)$$

The parameter Q_0 used in Lemma 26 gives an upper bound of the probability that a $\Theta(n, G, \alpha)$ -sequence S whose $\aleph(S)$ will not be similar enough to the original motif G according to the conditions in Lemma 26.

xvii. Select constant d_0 such that

$$n^3 c^{d_0 \log n} < \frac{1}{5 \cdot 2^x}. \quad (14)$$

xviii. Select constant d_1 such that $(v + u_1)c^{d_1 \log n} < \frac{1}{5 \cdot 2^x}$.

xix. Select number u_2 such that

$$(d_1 \log n)(v + u_1)\frac{c^{v+u_2}}{1-c} \leq \frac{1}{5 \cdot 2^x}, \text{ and} \quad (15)$$

$$(v + u_1)\frac{c^{v+u_2}}{1-c} < \frac{1}{5 \cdot 2^x} \quad (16)$$

Since only n is variable, we can make $u_2 = O(\log \log n)$.

xx. For a fixed $c \in (0, 1)$, define $\delta_c = \frac{\ln \frac{1}{c}}{2}$.

4.2. Description of Algorithm Recover-Motif

The algorithm is described in this section. Before presenting the algorithm, we define some notions.

Definition 9.

- Two sequences X_1 and X_2 are *weak left matched* if (1) both $|X_1|$ and $|X_2|$ are at least $d_0 \log n$, (2) $\text{diff}(X_1[1, i], X_2[1, i]) \leq \beta$ for all integers i , $v \leq i \leq d_0 \log n$.
- Two sequences X_1 and X_2 are *left matched* if (1) $d_0 \log n \leq |X_1|, |X_2|$, (2) $X_1[i] = X_2[i]$ for $i = 1, \dots, v-1$, and (3) $\text{diff}(X_1[1, i], X_2[1, i]) \leq \beta$ for all integers i , $v \leq i \leq d_0 \log n$.
- Two sequences X_1 and X_2 are *weak right matched* if X_1^R and X_2^R are weak left matched, where $X^R = a_n \cdots a_1$ is the inverse sequence of $X = a_1 \cdots a_n$.
- Two sequences X_1 and X_2 are *right matched* if X_1^R and X_2^R are left matched, where $X^R = a_n \cdots a_1$ is the inverse sequence of $X = a_1 \cdots a_n$.
- Two sequences X_1 and X_2 are *matched* if X_1 and X_2 are both left and right matched.

Variable L will be controlled in the range $L \in [(\log n)^{3+\epsilon_1}, n^{\frac{2}{5}-\epsilon_2}]$ in our algorithm with high probability. We define the following functions that depend on L .

Definition 10. Define $M(L) = \frac{\sqrt{3 \log n + x}}{\sqrt{1-\gamma}} \sqrt{L} \log n$. Define $M_1(L) = \frac{\delta_{c_0} M(L)}{\log n}$ (see Definition 8 for δ_c), where $c_0 = \frac{1}{4}$.

We would like to minimize the function $(\frac{n}{L} M + L^2) \log n$. This selection can make the total time complexity sublinear.

Definition 11. For a $\Theta_\alpha(n, G)$ sequence S , define $\text{LB}(S)$ to be the left boundary l of the motif region $\aleph(S)$ in S , and $\text{RB}(S)$ to be the right boundary r of the motif region $\aleph(S)$ in S such that $\aleph(S) = S[l, r]$.

4.2.1. Boundary-Phase of Algorithm Recover-Motif

The first phase of Algorithm Recover-Motif finds the rough motif boundaries of all input sequences. It first detects the rough motif boundaries of one sequence via comparing two input sequences. Then the rough boundaries of the first sequence is used to find the rough motif boundaries of other input sequences.

Three algorithms share most of the functions. We have a unified approach to describe them. A special variable “algorithm-type” selects one of the three algorithms, respectively.

Definition 12. Let algorithm-type represent one of the three algorithm types, “RANDOMIZED-SUBLINEAR”, “RANDOMIZED-SUBQUADRATIC”, and “DETERMINISTIC-SUPERQUADRATIC”.

Definition 13. Assume that A_1 is a set of positions in a $\Theta_\alpha(n, G)$ sequence S_1 and A_2 is a set of positions in a $\Theta_\alpha(n, G)$ sequence S_2 . If there is a position $a_1 \in A_1$ and $a_2 \in A_2$ such that for some position j with $1 \leq j \leq |G|$, a_1 is the position of $\aleph(S_1)[j]$ in S_1 and a_2 is the position of $\aleph(S_2)[j]$ in S_2 , then A_1 and A_2 have a *collision* at (a_1, a_2) .

In the following function Collision-Detection, the parameter $\omega \leq \beta$ is defined below in the three algorithms.

$$\omega_{\text{algorithm-type}} = \begin{cases} 0 & \text{if algorithm-type=RANDOMIZED-SUBLINEAR;} \\ \beta & \text{if algorithm-type=RANDOMIZED-SUBQUADRATIC;} \\ \beta & \text{if algorithm-type=DETERMINISTIC-SUPERQUADRATIC.} \end{cases} \quad (17)$$

Collision-Detection(S_1, U_1, S_2, U_2)

Input: a pair of $\Theta(n, G, \alpha)$ -sequences S_1 and S_2 , U_i is a set of locations in S_i for $i = 1, 2$.

Output: the left and right rough boundaries of two sequences.

Let D_1 be all subsequences $S_1[a, a + d_0 \log n - 1]$ of S_1 of length $d_0 \log n$ with $a \in U_1$.

Let D_2 be all subsequences $S_2[b, b + d_0 \log n - 1]$ of S_2 of length $d_0 \log n$ with $b \in U_2$.

Find two subsequences $X_1 = S_1[a_1, a_1 + d_0 \log n - 1] \in D_1$ and

$X_2 = S_2[b_1, b_1 + d_0 \log n - 1] \in D_2$ such that a_1 is the least and $\text{diff}(X_1, X_2) \leq \omega_{\text{algorithm-type}}$.

Find two subsequences $X'_1 = S_1[a'_1, a'_1 + d_0 \log n - 1] \in D_1$ and

$X'_2 = S_2[b'_1, b'_1 + d_0 \log n - 1] \in D_2$ such that a'_1 is the largest and

$\text{diff}(X'_1, X'_2) \leq \omega_{\text{algorithm-type}}$.

Find two subsequences $Y_1 = S_1[f_1, f_1 + d_0 \log n - 1] \in D_1$ and

$Y_2 = S_2[e_1, e_1 + d_0 \log n - 1] \in D_2$ such that e_1 is the least and

$\text{diff}(Y_1, Y_2) \leq \omega_{\text{algorithm-type}}$.

Find two subsequences $Y'_1 = S_1[f'_1, f'_1 + d_0 \log n - 1] \in D_1$ and

$Y'_2 = S_2[e'_1, e'_1 + d_0 \log n - 1] \in D_2$ such that e'_1 is the largest and

$\text{diff}(Y'_1, Y'_2) \leq \omega_{\text{algorithm-type}}$.

Return (a, a', e_1, e'_1) .

End of Collision-Detection

Function Point-Selection(S_1, S_2, L) will be defined differently in three different algorithms. It selects some positions from each interval of length L in both S_1 and S_2 .

Point-Selection(S, L, I)

Input: a pair of $\Theta(n, G, \alpha)$ -sequences S , a size parameter L of partition, and an interval of positions I in S .

Output: a set U of positions from S respectively.

Steps:

Let $U = \emptyset$.

If algorithm-type=RANDOMIZED-SUBLINEAR or RANDOMIZED-SUBQUADRATIC

If $(L \geq \frac{(\log n)^{3+\tau}}{100})$

For each interval I' in I , partition I' into intervals of size L .

Sample $M(L)$ random positions at every

interval of size L derived in the above partition, and put them into U .

Else

Put every position of I into U_1 .

If algorithm-type=DETERMINISTIC-SUPERQUADRATIC

Put every position of I into U .

Return U .

End of Point-Selection

Improve-Boundaries($S_1, a_l, a_r, S_2, f_l, f_r, L$)

Input: a $\Theta(n, G, \alpha)$ -sequence S_1 with rough left and right boundaries a_l and a_r , a $\Theta(n, G, \alpha)$ -sequences S_2 with rough left and right boundaries f_l and f_r , and the rough distance L to the nearest motif boundary from those rough boundaries.

Output: improved rough left and right boundaries for both S_1 and S_2 .

Steps:

Find two subsequences $X_1 = S_1[a_1, a_1 + d_0 \log n - 1]$ and $X_2 = S_2[b_2, b_2 + d_0 \log n - 1]$ with $a_1 \in [a_l - L, a_l + L]$ and $b_2 \in [f_l - L, f_l + L]$ such that $\text{diff}(X_1, X_2) \leq \beta$ and a_1 is the least.

Find two subsequences $X'_1 = S_1[a'_1, a'_1 + d_0 \log n - 1]$ and $X'_2 = S_2[b'_2, b'_2 + d_0 \log n - 1]$ with $a'_1 \in [a_r - L, a_r + L]$ and $b'_2 \in [f_r - L, f_r + L]$ such that $\text{diff}(X'_1, X'_2) \leq \beta$ and a'_1 is the largest.

Find two subsequences $Y_1 = S_1[e_1, e_1 + d_0 \log n - 1]$ and $Y_2 = S_2[f_2, f_2 + d_0 \log n - 1]$ with $e_1 \in [a_l - L, a_l + L]$ and $f_2 \in [f_l - L, f_l + L]$ such that $\text{diff}(Y_1, Y_2) \leq \beta$ and f_2 is the least.

Find two subsequences $Y'_1 = S_1[e'_1, e'_1 + d_0 \log n - 1]$ and $Y'_2 = S_2[f'_2, f'_2 + d_0 \log n - 1]$ with $e'_1 \in [a_r - L, a_r + L]$ and $f'_2 \in [f_r - L, f_r + L]$ such that $\text{diff}(Y'_1, Y'_2) \leq \beta$ and f'_2 is the largest.

Return (a_1, a'_1, f_2, f'_2) .

End of Improve-Boundaries

Initial-Boundaries(S_1, S_2)

Input: a pair of $\Theta(n, G, \alpha)$ -sequences S_1 and S_2

Output: rough left boundary roughLeft_{S_1} of S_1 , right boundary roughRight_{S_1} of S_1 , rough left boundary roughLeft_{S_2} of S_2 , and right boundary roughRight_{S_2} of S_2 .

Steps:

Let $U_1 = U_2 = \emptyset$.

Let $L = n^{2/5}$.

Repeat

Let $U_1 = \text{Point-Selection}(S_1, L, [1, |S_1|])$.

Let $U_2 = \text{Point-Selection}(S_2, L, [1, |S_2|])$.

Let $(L_{S_1}, R_{S_1}, L_{S_2}, R_{S_2}) = \text{Collision-Detection}(S_1, U_1, S_2, U_2)$.

If $(L_{S_1} \neq \emptyset \text{ and } R_{S_1} \neq \emptyset)$

Then Goto H.

Else $L = L/2$.

Until $(L < \frac{1}{2} \frac{(\log n)^{3+\tau}}{100})$

H: Return $\text{Improve-Boundaries}(S_1, L_{S_1}, R_{S_1}, S_2, L_{S_2}, R_{S_2}, 2L)$.

End of Initial-Boundaries

Motif-Length-And-Boundaries(Z_1)

Input: $Z_1 = \{S'_1, \dots, S'_{2k_1}\}$ is a set of independent $\Theta(n, G, \alpha)$ sequences.

Steps:

For $i = 1$ to k_1

let $(\text{roughLeft}_{S'_{2i-1}}, \text{roughRight}_{S'_{2i}}) = \text{Initial-Boundaries}(S'_{2i-1}, S'_{2i})$.

Let L_1 be the median of $\cup_{i=1}^{k_1} \{(\text{roughRight}_{S'_{2i-1}} - \text{roughLeft}_{S'_{2i-1}})\}$.

Return L_1 .

End of Motif-Length-And-Boundaries

4.2.2. Extract-Phase of Algorithm Recover-Motif

After a set of motif candidates W is produced from Boundary-Phase of algorithm Recover-Motif, we use this set to match with another set of input sequences to recover the hidden motif by voting.

Match(G_l, G_r, S_i)

Input: a motif left part G_l (which can be derived from the rough left boundary of an input sequence S), a motif right part G_r , a sequence S_i'' from the group Z_2 , with known rough left and right boundaries.

Output: either a rough motif region of S_i'' , or an empty sequence which means the failure in extracting the motif region $\aleph(S_i'')$ of S_i'' .

Steps:

Find a position a in S_i'' with $\text{roughLeft}_{S_i''} \leq a \leq \text{roughLeft}_{S_i''} + (v + u_2)$.

such that G_l and $S_i''[a, a + |G_l| - 1]$ are left matched (see Definition 9).

Find a position b in S_i'' with $\text{roughRight}_{S_i''} - (v + u_2) \leq b \leq \text{roughRight}_{S_i''}$

such that G_r and $S_i''[b - |G_r| + 1, b]$ are right matched (see Definition 9).

If both a and b are found

Then output $S_i''[a, b]$

Else output \emptyset (empty string).

End of Match

Extract(G_l, G_r, Z_2):

Input $Z_2 = \{S_1'', S_2'', \dots, S_{k_2}''\}$ and their rough left boundaries and rough right boundaries.

Steps:

For each S_i'' with $i = 1, 2, \dots, k_2$,

let $G_i'' = \text{Match}(G_l, G_r, S_i'')$.

Return $(G_1'', G_2'', \dots, G_{k_2}'')$.

End of Extract

The following is Extract-Phase of algorithm Recover-Motif. It extracts the motif regions of another set Z_2 of input sequences.

Extract-Phase(S', Z_2):

Input S' is an input sequence with known $\text{roughLeft}_{S'}$ and $\text{roughRight}_{S'}$ for its rough left and right boundaries respectively, and $Z_2 = \{S_1'', \dots, S_{k_2}''\}$ is a set of input sequences.

Steps:

For each subsequence $G_l = S'[a, a + d_0 \log n - 1]$ with $a \in [\text{roughLeft}_{S'}, \text{roughLeft}_{S'} + (v + u_1)]$

and $G_r = S'[b - d_0 \log n + 1, b]$ with $b \in [\text{roughRight}_{S'} - (v + u_1), \text{roughRight}_{S'}]$

let $(G_1'', G_2'', \dots, G_{k_2}'')$ be the output from $\text{Extract}(G_l, G_r, Z_2)$.

If the number of empty sequences in G_1'', \dots, G_{k_2}'' is at most $(Q_0 + (R + 2\epsilon))k_2$

Then return $(G_1'', G_2'', \dots, G_{k_2}'')$.

Return \emptyset (empty set).

End of Extract-Phase

4.2.3. Voting-Phase

The function $\text{Vote}(G_1'', G_2'', \dots, G_{k_2}'')$ is to generate another sequence G' by voting, where $G'[i]$ is the most frequent character among $G_1''[i], G_2''[i], \dots, G_{k_2}''[i]$.

Voting-Phase($G_1'', G_2'', \dots, G_{k_2}''$)

Input: $\Theta(n, G, \alpha)$ sequences $G_1'', G_2'', \dots, G_{k_2}''$ of the same length m .

Output: a sequence G' , which is derived by voting on every position of the input sequences.

Steps:

For each $j = 1, \dots, m$

let a_j be the most frequent character among $G_1''[j], \dots, G_{k_2}''[j]$.

Return $G' = a_1 \dots a_m$.

End of Vote

4.2.4. Entire Algorithm Recover-Motif

The entire algorithm is described below. We maintain the size of Z_1 and Z_2 to be roughly equal, which implies

$$|Z_1| = \Theta(|Z_2|) \quad (18)$$

Algorithm Recover-Motif (Z)

Input: $Z = Z_1 \cup Z_2$, where $Z_1 = \{S'_1, \dots, S'_{k_1}\}$ and $Z_2 = \{S''_1, \dots, S''_{k_2}\}$ are two sets of input sequences.

Steps:

Preprocessing Part:

For each $S \in Z_1 \cup Z_2$, let $\text{roughLeft}_S = \text{roughRight}_S = 0$ (the two boundaries are unknown).

$l_{\text{motif}} = \text{MotifLengthAndBoundaries}(Z_1)$.

Let $L = l_{\text{motif}}/4$.

For $i = 1$ to k_1 ,

let $U_{S'_{2i-1}} = \text{Point-Selection}(S'_{2i-1}, L, [\text{roughLeft}_{S'_{2i-1}} - 2L, \text{roughLeft}_{S'_{2i-1}} + 2L]) \cup$
 $\text{Point-Selection}(S'_{2i-1}, L, [\text{roughRight}_{S'_{2i-1}} - 2L, \text{roughRight}_{S'_{2i-1}} + 2L]).$

For $j = 1$ to k_2

let $U_{S''_j} = \text{Point-Selection}(S''_j, L, [1, |S''_j|]).$

For $i = 1$ to k_1

For each $S''_j \in Z_2$

Let $(L_{S'_{2i-1}}, R_{S'_{2i-1}}, L_{S''_j}, R_{S''_j}) = \text{Collision-Detection}(S'_{2i-1}, U_{S'_{2i-1}}, S''_j, U_{S''_j}).$

Let $(L_{S'_{2i-1}}, R_{S'_{2i-1}}, \text{roughLeft}_{S''_j}, \text{roughRight}_{S''_j}) =$

$\text{Improve-Boundaries}(S'_{2i-1}, L_{S'_{2i-1}}, R_{S'_{2i-1}}, S''_j, L_{S''_j}, R_{S''_j}, 2L).$

Let $(G''_1, G''_2, \dots, G''_{k_2})$ be the output from $\text{Extract-Phase}(S'_{2i-1}, Z_2).$

If $(G''_1, G''_2, \dots, G''_{k_2})$ is not empty

Then go to Voting Part.

Voting Part:

Return $\text{Voting-Phase}(G''_1, G''_2, \dots, G''_{k_2}).$

End of Algorithm Recover-Motif

5. Analysis of Algorithm

The correctness of the algorithm will be proved via a series of Lemmas in Sections 5.2 and 5.3. Section 5.2 is for Boundary-Phase and Section 5.3 is for Extract-Phase. Furthermore, Section 5.3 gives some lemma for the two randomized algorithms and Section 5.5 gives the proof for the deterministic algorithm.

5.1. Review of Some Classical Results in Probability

Some well known results in classical probability theory are listed. The readers can skip this section if they understand them well. The inclusion of these results make the paper self-contained.

- For a list of events A_1, \dots, A_m , $\Pr[A_1 \cup A_2 \cup \dots \cup A_m] \leq \Pr[A_1] + \Pr[A_2] + \dots + \Pr[A_m]$.
- For two independent events A and B , $\Pr[A \cap B] = \Pr[A]\Pr[B]$.
- For a random variable Y , $\Pr[Y \geq t] \leq \frac{E[Y]}{t}$ for all positive real number t . This is called Markov inequality.

The analysis of our algorithm employs the Chernoff bound [17] and Corollary 17 below, which can be derived from it (see [14]).

Theorem 14 ([17]). *Let X_1, \dots, X_n be n independent random 0-1 variables, where X_i takes 1 with probability p_i . Let $X = \sum_{i=1}^n X_i$, and $\mu = E[X]$. Then for any $\delta > 0$,*

$$i. \Pr(X < (1 - \delta)\mu) < e^{-\frac{1}{2}\mu\delta^2}, \text{ and}$$

$$ii. \Pr(X > (1 + \delta)\mu) < \left[\frac{e^\delta}{(1+\delta)} \right]^\mu.$$

We follow the proof of Theorem 14 to make the following version of Chernoff bound so that it can be used in our algorithm analysis.

Theorem 15. *Let X_1, \dots, X_n be n independent random 0-1 variables, where X_i takes 1 with probability at most p . Let $X = \sum_{i=1}^n X_i$. Then for any $\delta > 0$, $\Pr(X > (1 + \delta)pn) < \left[\frac{e^\delta}{(1+\delta)} \right]^{pn}$.*

Proof: Let y be an arbitrary positive real number. By the definition of expectation, we have $E(e^{yX_i}) = \Pr(X_i = 1)e^y + \Pr(X_i = 0)$. Since the function $f(x) = xe^y + (1 - x)$ is increasing for all $y > 0$ and $\Pr(X_i = 1) \leq p$, we have $E(e^{yX_i}) \leq pe^y + (1 - p)$. We have the following inequalities:

$$\Pr(X > (1 + \delta)pn) < \frac{E(e^{yX})}{e^{y(1+\delta)pn}} \tag{19}$$

$$\leq \frac{\prod_{i=1}^n E(e^{yX_i})}{e^{y(1+\delta)pn}} \tag{20}$$

$$= \frac{\prod_{i=1}^n (pe^y + 1 - p)}{e^{y(1+\delta)pn}} \tag{21}$$

$$= \frac{\prod_{i=1}^n (1 + p(e^y - 1))}{e^{y(1+\delta)pn}} \tag{22}$$

$$\leq \frac{\prod_{i=1}^n e^{p(e^y - 1)}}{e^{y(1+\delta)pn}} \tag{23}$$

$$= \frac{e^{(e^y - 1)pn}}{e^{y(1+\delta)pn}} \tag{24}$$

$$= \left(\frac{e^{(e^y - 1)}}{e^{y(1+\delta)}} \right)^{pn}. \tag{25}$$

The inequality (19) is based on Markov inequality. The transition from (20) to (21) is due to the independence of those variables X_1, \dots, X_n .

Since $\left(\frac{e^{(e^y - 1)}}{e^{y(1+\delta)}} \right)$ is minimal at $y = \ln(1 + \delta)$, we have $\Pr(X > (1 + \delta)pn) < \left[\frac{e^\delta}{(1+\delta)} \right]^{pn}$. ■

Define $g(\delta) = \frac{e^\delta}{(1+\delta)^{(1+\delta)}}$. We note that $g(\delta)$ is always strictly less than 1 for all $\delta > 0$, and $g(\delta)$ is fixed if δ is a constant. This can be verified by checking that the function $f(x) = \ln \frac{e^x}{(1+x)^{(1+x)}} = x - (1+x) \ln(1+x)$ is decreasing and $f(0) = 0$. This is because $f'(x) = -\ln(1+x)$, which is less than 0 for all $x > 0$.

Theorem 16. *Let X_1, \dots, X_n be n independent random 0-1 variables, where X_i takes 1 with probability at most p . Let $X = \sum_{i=1}^n X_i$. Then for any $\delta > 0$, $\Pr(X > (1-\delta)pn) < e^{-\frac{1}{2}pn\delta^2}$.*

Proof: $\Pr[X < (1-\delta)pn] = \Pr[-X > -(1-\delta)pn] = \Pr[e^{-yX} > e^{-y(1-\delta)pn}]$ for each real number y . Applying Markov inequality, we have

$$\Pr[X < (1-\delta)pn] < \frac{\prod_{i=1}^n E(e^{-yX_i})}{e^{-y(1-\delta)np}} \quad (26)$$

$$< \frac{e^{(e^{-y}-1)np}}{e^{-y(1-\delta)np}} \quad (27)$$

$$< \left(\frac{e^{-\delta}}{(1-\delta)^{1-\delta}} \right)^{pn} \quad (28)$$

$$< e^{-\frac{1}{2}pn\delta^2}. \quad (29)$$

The transition from (26) to (27) is to let $t = \ln \frac{1}{1-\delta}$. The transition from (28) to (29) follows from the fact $(1-\delta)^{1-\delta} > e^{-\delta+\delta^2/2}$. ■

Corollary 17 ([14]). *Let X_1, \dots, X_n be n independent random 0-1 variables and $X = \sum_{i=1}^n X_i$.*

- i. If X_i takes 1 with probability at most p , then for any $\frac{1}{3} > \epsilon > 0$, $\Pr(X > pn + \epsilon n) < e^{-\frac{1}{3}n\epsilon^2}$.*
- ii. If X_i takes 1 with probability at least p , then for any $\epsilon > 0$, $\Pr(X < pn - \epsilon n) < e^{-\frac{1}{2}n\epsilon^2}$.*

Proof: For $X = \sum_{i=1}^n X_i$, $\mu = E(X) = \sum_{i=1}^n E(X_i) = pn$. Let $\delta = \frac{\epsilon}{p}$. (1) follows from Theorem 14. By Taylor theorem, $\ln(1+\epsilon) \geq \epsilon - \frac{\epsilon^2}{2}$. We have that $(1+\frac{1}{\epsilon}) \ln(1+\epsilon) \geq (1+\frac{1}{\epsilon})(\epsilon - \frac{\epsilon^2}{2}) = 1 + \frac{\epsilon}{2} - \frac{\epsilon^2}{2} > 1 + \frac{\epsilon}{3}$. Thus, $\frac{e}{(1+\epsilon)^{(1+\frac{1}{\epsilon})}} < e^{-\frac{\epsilon}{3}}$. Since $pn + \epsilon n = (1+\delta)\mu$ and the function $(1+y)^{\frac{1}{y}}$ is increasing for $y > 0$,

$$\Pr(X > pn + \epsilon n) = \Pr(X > (1+\delta)\mu) < \left[\frac{e^{\frac{\epsilon}{p}}}{(1+\frac{\epsilon}{p})^{(1+\frac{\epsilon}{p})}} \right]^{pn} = \left[\frac{e}{(1+\frac{\epsilon}{p})^{(1+\frac{p}{\epsilon})}} \right]^{\epsilon n} \leq \left[\frac{e}{(1+\epsilon)^{(1+\frac{1}{\epsilon})}} \right]^{\epsilon n} \leq e^{-\frac{\epsilon^2 n}{3}}.$$

Thus (ii) is proved. ■

5.2. Analysis of Boundary-Phase of Algorithm Recover-Motif

Lemma 18 shows that with only small probability, a sequence can match a random sequence. It will be used to prove that when two substrings in two different $\Theta(n, G, \alpha)$ -sequences are similar, they are unlikely not to coincide with the motif regions in the two $\Theta(n, G, \alpha)$ -sequences, respectively.

Lemma 18. *Assume that X_1 and X_2 are two independent sequences of the same length and that every character of X_2 is a random character from Σ . Then*

- i. if $1 \leq |X_1| = |X_2| < v$, then the probability that X_1 and X_2 are matched is $\leq \frac{1}{t^{|X_1|}}$ ($t = ||\Sigma||$); and*

- ii. the probability for $\text{diff}(X_1, X_2) \leq \beta$ is at most $e^{-\frac{\epsilon^2 |X_1|}{3}}$.*

Proof: The two statements are proved as follows.

Statement i: For every character $X_2[j]$ with $1 \leq j < v$, the probability is $\frac{1}{t}$ that $X_2[j] = X_1[j]$.

Statement ii: For every character $X_2[j]$ with $1 \leq j \leq |X_2|$, the probability is $\frac{1}{t}$ for $X_2[j]$ to equal $X_1[j]$. If $\text{diff}(X_1, X_2) \leq \beta$, the two sequences X_1 and X_2 are identical at least $(1 - \beta)|X_1|$ positions, but the expected number of positions where the two sequences are identical is $\frac{1}{t}|X_1|$.

The probability for $\text{diff}(X_1, X_2) \leq \beta$ is at most $e^{-\frac{(1-\beta-\frac{1}{t})^2}{3}|X_1|} \leq e^{-\frac{\epsilon^2}{3}|X_1|}$ by Corollary 17, and Definitions 8 and 9. \blacksquare

Lemma 19 shows that with small probability, an input $\Theta_\alpha(n, G)$ sequence contains motif region that has many mutations.

Lemma 19. *With probability at most $\frac{c^y}{1-c}$, a $\Theta_\alpha(n, G)$ sequence S changes more than $\frac{\beta}{2}t$ characters in its first left t motif region $\aleph(S)$ for some t with $y \leq t \leq |G|$, where $c = e^{-\frac{\epsilon^2}{3}}$.*

Proof: Every character in the $\aleph(S)$ region has probability at most α to mutate. We know that $|\aleph(S)| = |G| \geq d$. By Corollary 17, with probability at most $e^{-\frac{\epsilon^2}{3}t}$, a sequence S in Z_1 has more than $(\alpha + \epsilon)t$ mutations (recall the setting for β at Definition 9) among the first left t characters. The total is $\sum_{t=y}^{\infty} e^{-\frac{\epsilon^2}{3}t} = \frac{c^y}{1-c}$. \blacksquare

Lemma 20 shows that Improve-Boundaries() has good chance to improve the accuracy of rough motif boundaries.

Lemma 20. *Assume that $\Theta_\alpha(n, G)$ sequence S_i has $L_{S_i} \in [\text{LB}(S_i) - L, \text{LB}(S_i) + L]$ and $R_{S_i} \in [\text{RB}(S_i) - L, \text{RB}(S_i) + L]$ for $i = 1, 2$. Then for $(\text{roughLeft}_{S_1}, \text{roughRight}_{S_1}, \text{roughLeft}_{S_2}, \text{roughRight}_{S_2}) = \text{Improve-Boundaries}(S_1, L_{S_1}, R_{S_1}, S_2, L_{S_2}, R_{S_2}, L)$, we have the following two facts:*

- i. *With probability at most $\frac{2c^v}{1-c} + \frac{2(v+u)c^{v+u}}{(1-c)^2} + \frac{1}{5 \cdot 2^{x_n}}$, roughLeft_{S_i} is not in $[\text{LB}(S_i) - (v+u), \text{LB}(S_i)]$ for $i = 1, 2$.*
- ii. *With probability at most $\frac{2c^v}{1-c} + \frac{2(v+u)c^{v+u}}{(1-c)^2} + \frac{1}{5 \cdot 2^{x_n}}$, roughRight_{S_i} is not in $[\text{RB}(S_i), \text{RB}(S_i) + (v+u)]$ for $i = 1, 2$.*
- iii. *Improve-Boundaries($S_1, L_{S_1}, R_{S_1}, S_2, L_{S_2}, R_{S_2}, L$) runs in $O(L^2 \log n)$ time.*

Proof: We need a bound for the following inequality:

$$\sum_{i=j}^{\infty} ia^i < \frac{ja^j}{(1-a)^2}. \quad (30)$$

Let $f(x) = \sum_{i=j}^{\infty} e^{\theta ix}$. Compute the derivative $f'(x) = \theta \sum_{i=j}^{\infty} ie^{\theta ix}$. We also have the closed form for the function $f(x) = \frac{e^{\theta jx}}{1 - e^{\theta x}}$, which implies

$$f'(x) = \frac{\theta j e^{\theta jx} (1 - e^{\theta x}) - e^{\theta jx} (-\theta e^{\theta x})}{(1 - e^{\theta x})^2} \quad (31)$$

$$= \frac{\theta j e^{\theta jx} - \theta(j-1)e^{\theta(j+1)x}}{(1 - e^{\theta x})^2}. \quad (32)$$

Let $\theta = \ln a$ and $x = 1$. We have $\sum_{i=j}^{\infty} ia^i = \frac{ja^j - (j-1)a^{j+1}}{(1-a)^2} < \frac{ja^j}{(1-a)^2}$.

Statement i. By Lemma 19, with probability at most $2\frac{c^v}{1-c}$, one of the left motif first y characters region of S_i will change $\frac{\beta}{2}y$ characters. Therefore, with probability at most $P_1 = 2\frac{c^v}{1-c}$, $\text{roughLeft}_{S_i} > \text{LB}(S_i)$.

For a pair of positions p in S_1 and q in S_2 , without loss generality, assume that p has larger distance to the left boundary $\text{LB}(S_1)$ of S_1 than q to the left boundary $\text{LB}(S_2)$ of S_2 . Let $v + y$ be the distance from p to the left boundary $\text{LB}(S_1)$ of S_1 .

By Lemma 18, the probability is at most c^{v+y} that there will be a match. There are at most $(v + y)$ cases for q . With probability is at most $P_2 = 2 \sum_{y=u}^{\infty} (v + y)c^{v+y} < \frac{2(v+u)c^{v+u}}{(1-c)^2}$ by inequality (30), $\text{roughLeft}_{S_1} < \text{LB}(S_1) - (v + u)$.

For the cases that one position is in random region and has distance more than $d_0 \log n$ with the left boundary, the probability is at most $P_3 = n^2 c^{d_0 \log n} < \frac{1}{5 \cdot 2^{x_n}}$ by inequality (14).

Therefore, we have total probability at most $P_1 + P_2 + P_3$ that roughLeft_{S_1} is not in $[\text{LB}(S_1) - (v + u), \text{LB}(S_1)]$.

Statement ii. One can also provide a symmetric analogous proof for this statement.

Statement iii. The computation time easily follows from the implementation of ImproveBoundaries($S_1, L_{S_1}, R_{S_1}, S_2, L_{S_2}, R_{S_2}$). ■

Lemma 21. Assume that for each L with $0 < L \leq \frac{|G|}{2}$, with probability at most $\varsigma(n)$, $L_{S_i} \notin [\text{LB}_{S_i} - L, \text{LB}_{S_i} + L]$ for $i = 1, 2$, where $(L_{S_1}, R_{S_1}, L_{S_2}, R_{S_2}) = \text{Collision-Detection}(S_1, U_1, S_2, U_2)$, $U_1 = \text{Point-Selection}(S_1, L)$, and $U_2 = \text{Point-Selection}(S_2, L)$. Then with probability at most $\varsigma(n) + \frac{2(v+u_1)c^{v+u_1}}{(1-c)^2} + \frac{c^v}{1-c} + \frac{1}{5 \cdot 2^{x_n}}$, Initial-Boundary(S_1, S_2) returns $(L_{S_1}, R_{S_1}, L_{S_2}, R_{S_2})$ with $L_{S_i} \notin [\text{LB}(S_i) - (v + u_1), \text{LB}(S_i)]$ or $R_{S_i} \notin [\text{RB}(S_i), \text{RB}(S_i) + (v + u_1)]$ for $i = 1, 2$;

Proof: It follows from Lemma 20. ■

Lemma 22. Assume that with probability $p < 0.5$, each S'_{2i-1} has its rough boundaries $\text{roughLeft}_{S'_{2i-1}} \notin [\text{LB}(S'_{2i-1}) - u, \text{LB}(S'_{2i-1})]$ or $\text{roughRight}_{S'_{2i-1}} \notin [\text{RB}(S'_{2i-1}), \text{RB}(S'_{2i-1}) + u]$, then with probability at most $e^{-(0.5-p-\epsilon)^2 k_1/3}$, l_{motif} is not in $[|G| - 2u, |G| + 2u]$, where l_{motif} is selected as median of $\cup_{i=1}^{k_1} \{(\text{roughRight}_{S'_{2i-1}} - \text{roughLeft}_{S'_{2i-1}})\}$.

Proof: If both $\text{roughLeft}_{S'_{2i-1}} \in [\text{LB}(S'_{2i-1}) - u, \text{LB}(S'_{2i-1})]$ and $\text{roughRight}_{S'_{2i-1}} \in [\text{RB}(S'_{2i-1}), \text{RB}(S'_{2i-1}) + u]$, then $(\text{roughRight}_{S'_{2i-1}} - \text{roughLeft}_{S'_{2i-1}})$ is in $[|G| - 2u, |G| + 2u]$.

If the median of $\cup_{i=1}^{k_1} \{(\text{roughRight}_{S'_{2i-1}} - \text{roughLeft}_{S'_{2i-1}})\}$ is not in $[|G| - 2u, |G| + 2u]$, then there are at least $\lfloor k_1 \rfloor$ is to have $\text{roughLeft}_{S'_{2i-1}} \notin [\text{LB}(S'_{2i-1}) - u, \text{LB}(S'_{2i-1})]$ or $\text{roughRight}_{S'_{2i-1}} \notin [\text{RB}(S'_{2i-1}), \text{RB}(S'_{2i-1}) + u]$.

On the other hand, the probability is at most p , $\text{roughLeft}_{S'_{2i-1}} \notin [\text{LB}(S'_{2i-1}) - u, \text{LB}(S'_{2i-1})]$ or $\text{roughRight}_{S'_{2i-1}} \notin [\text{RB}(S'_{2i-1}), \text{RB}(S'_{2i-1}) + u]$. So, this lemma follows from Corollary 17. ■

For a $\Theta(n, G, \alpha)$ -sequence S , we often obtain its left rough boundary with $\text{roughLeft}_S \leq \text{LB}(S)$. Some times its exactly left boundary may be miss in the algorithm.

Definition 23.

- A $\Theta(n, G, \alpha)$ -sequence S misses its left boundary if $\text{roughLeft}_S > \text{LB}(S)$.
- A $\Theta(n, G, \alpha)$ -sequence S misses its right boundary if $\text{roughRight}_S < \text{RB}(S)$.

Definition 24.

- A $\Theta(n, G, \alpha)$ -sequence S contains a *left half stable* motif region $\aleph(S)$ if $\text{diff}(G'[1, h], G[1, h]) \leq \frac{\beta}{2}$ for all $h = v, v+1, \dots, m$, where $G' = \aleph(S)$, $c = e^{-\frac{\epsilon^2}{3}}$ and $m = |G|$ as defined in Definition 8 and Section 2, respectively.
- A $\Theta(n, G, \alpha)$ -sequence S contains a *right half stable* motif region $\aleph(S)$ if $\text{diff}(G'[m-h, m], G[m-h, m]) \leq \frac{\beta}{2}$ for $h = v-1, v+1, \dots, m-1$, where $G' = \aleph(S)$ and $m = |G|$.
- A $\Theta(n, G, \alpha)$ -sequence S contains a *stable* motif region $\aleph(S)$ satisfying the following conditions: (1) $G'[i] = G[i]$ for $i = 1, \dots, v-1$; (2) $G'[m-i+1] = G[m-i+1]$ for $i = 1, \dots, v-1$; (3) S motif region is both left and right half stable, where $G' = \aleph(S)$ and $m = |G|$.

Lemma 25. Assume that

- $l_{\text{motif}} \in [|G| - 2(v + u_1), |G| + 2(v + u_1)]$;
- S contains a both left half and right half stable motif region and $\text{roughLeft}_S \in [\text{LB}(S) - (v + u_1), \text{LB}(S)]$ and $\text{roughRight}_S \in [\text{RB}(S), \text{RB}(S) + (v + u_1)]$ (see Definition 8 for u_1 and v); and
- for each L with $(v + u_1) < L \leq \frac{|G|}{2}$, if S_1 has $\text{roughLeft}_{S_1} \notin [\text{LB}_{S_1} - L, \text{LB}_{S_1} + L]$ and $\text{roughRight}_{S_1} \notin [\text{RB}_{S_1} - L, \text{RB}_{S_1} + L]$, then with probability at most $\varsigma(n)$, $L_{S_i''} \notin [\text{LB}_{S_i''} - 2L, \text{LB}_{S_i''} + 2L]$ for $i = 1, 2$, where $(L_{S_1}, R_{S_1}, L_{S_1''), R_{S_1''}) = \text{Collision-Detection}(S_1, U_1, S_i'', U_2)$, $U_1 = \text{Point-Selection}(S_1, L, [\text{roughLeft}_{S_1} - 2L, \text{roughLeft}_{S_1} + 2L]) \cup \text{Point-Selection}(S_1, L, [\text{roughRight}_{S_1} - 2L, \text{roughRight}_{S_1} + 2L])$, and $U_2 = \text{Point-Selection}(S_i'', L, [1, |S_i''|])$.
- The rough boundaries for all sequences $S_i'' \in Z_2$ are computed via $(L_S, R_S, L_{S_i''}, R_{S_i''}) = \text{Collision-Detection}(S, U_S, S_i'', U_{S_i''})$, and $(L_S, R_S, \text{roughLeft}_{S_i''}, \text{roughRight}_{S_i''}) = \text{Improve-Boundaries}(S, L_S, R_S, S_i'', L_{S_i''}, R_{S_i''}, 2L)$.

Then with probability at most $e^{-\frac{\epsilon^2 k_2}{3}}$, there are more than $(2(\varsigma(n) + (v + u_1)\frac{e^{v+u}}{1-c} + \frac{c^v}{1-c}) + \epsilon)k_2$ sequences S_i'' in $\{S_1'', \dots, S_{k_2}''\}$ with $\text{roughLeft}(S_i'') \notin [\text{LB}(S_i'') - (v + u), \text{LB}(S_i'')]$ or $\text{roughRight}(S_i'') \notin [\text{RB}(S_i''), \text{RB}(S_i'') + (v + u)]$.

Proof: According to the condition of this lemma, with probability at most $P_1 = \varsigma(n)$, $L_{S_i''} \notin [\text{LB}_{S_i''} - 2L, \text{LB}_{S_i''} + 2L]$, where $(L_S, R_S, L_{S_i''}, R_{S_i''}) = \text{Collision-Detection}(S, U_1, S_i'', U_2)$ and $(U_1, U_2) = \text{Point-Selection}(S, S_i'', L)$.

For a fix pattern from S , by Lemma 18, with probability at most $\sum_{y=v+u}^{\infty} c^y = \frac{c^{v+u}}{1-c}$, it has distance more than $v + u$ to the true left boundary. As we need to deal with $v + u_1$ possible patterns from S , with probability at most $P_{2,l} = (v + u_1)\frac{e^{v+u}}{1-c}$, $\text{roughLeft}_{S_i''} < \text{LB}(S_i'') - (v + u)$.

Similarly, with probability at most $P_{2,r} = (v + u_1)\frac{e^{v+u}}{1-c}$, $\text{roughRight}_{S_i''} < \text{RB}(S_i'') + (v + u)$. Let $P_2 = P_{2,l} + P_{2,r}$.

With probability at most $P_{3,l} = \frac{c^v}{1-c}$, S_i'' does not contain a left half stable motif region by Lemma 19. Similarly, with probability at most $P_{3,r} = \frac{c^v}{1-c}$, S_i'' does not contain a right half stable motif region. Let $P_3 = P_{3,l} + P_{3,r}$.

Although S is involved to search the left boundary with all other sequences. The non-missing condition is to let each sequence do not change too many characters in the motif region. Therefore, this is an independent event for each sequence. It is safe to use Chernoff bound to deal with it.

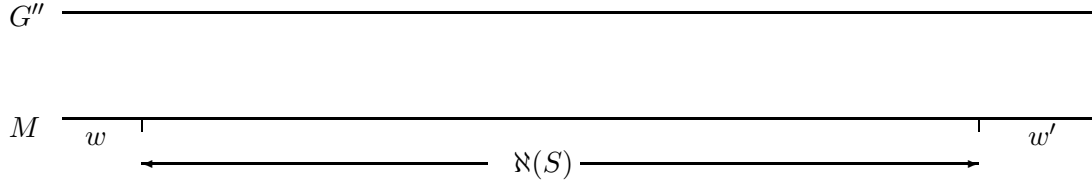


Figure 1: G'' and M

With probability at most $P = e^{-\frac{\epsilon^2 k_2}{3}}$, there are more than $(P_1 + P_2 + P_3 + \epsilon)k_2$ sequences S''_i in $\{S''_1, \dots, S''_{k_2}\}$ with $\text{roughLeft}(S''_i) \notin [\text{LB}(S''_i) - (v + u), \text{LB}(S''_i)]$ or $\text{roughRight}(S''_i) \notin [\text{RB}(S''_i), \text{RB}(S''_i) + (v + u)]$. ■

5.3. Analysis of Extract-Phase and Voting-Phase of Algorithm Recover-Motif

Lemma 26 shows that with high probability, the left and last parts of the motif region in a $\Theta(n, G, \alpha)$ -sequence do not change much.

Lemma 26. *With probability at most Q_0 , a $\Theta(n, G, \alpha)$ -sequence S does not contain a stable motif region.*

Proof: The probability is $V_1 = 2(v - 1)\alpha$ not to satisfy conditions (1) and (2) of Definition 24. Consider condition (3). Since every character of $\mathcal{N}(S)[1, m]$ (notice that $m = |G|$) has probability at most α to mutate, by Corollary 17, the probability is at most $e^{-\frac{1}{3}\epsilon^2 r}$ that $\text{diff}(G[1, h], G'[1, h]) > \frac{\beta}{2} = \alpha + \epsilon$. Let $V_3 = \sum_{r=v}^{\infty} e^{-\frac{1}{3}\epsilon^2 r} = \frac{c^v}{1-c}$, where $c = e^{-\frac{1}{3}\epsilon^2}$ as defined in Definition 8. Therefore, the probability is at most V_3 that $\text{diff}(G[1, h], G'[1, h]) > \frac{\beta}{2} = \alpha + \epsilon$ for some $h \in \{v, v + 1, \dots, m\}$. Similarly we define $V_4 = \sum_{r=v}^{\infty} e^{-\frac{1}{3}\epsilon^2 r} \leq \frac{c^v}{1-c}$ for the probability on the right-hand side. The probability is at most V_4 that $\text{diff}(G[m - h, m], G'[m - h, m]) > \frac{\beta}{2} = \alpha + \epsilon$ for some $h \in \{v, v + 1, \dots, m\}$. The probability that S does not contain a stable motif region is at most $V_1 + V_3 + V_4 = Q_0$. ■

Definition 27. Assume that $Z_1 = \{S'_1, \dots, S'_{2k_1}\}$ contains S'_{2i-1} that contains a stable motif region. We fix such a S'_{2i-1} .

- Define $G_L = \mathcal{N}(S'_{2i-1})[1, d_0 \log n - 1]$ to be the left part of the motif region $\mathcal{N}(S'_{2i-1})$.
- Define $G_R = \mathcal{N}(S'_{2i-1})[|G| - (d_0 \log n) + 1, |G|]$ to be the right part of the motif region $\mathcal{N}(S'_{2i-1})$.

Lemma 28 shows that with high probability, Extract-Phase of algorithm Recover-Motif extracts the correct motif regions from the sequences in Z_1 . It uses G'' to match $\mathcal{N}(S)$ in another sequences S . The parameter R gives a small probability that the matched region between G'' and S is not in $\mathcal{N}(S)$.

Lemma 28.

i. Assume that G_l and G_r are fixed sequences of length $d_0 \log n$. Let S be a $\Theta(n, G, \alpha)$ -sequence with $M \in \text{Match}(G_l, G_r, S)$ and let w_0 be the number of characters of M that are not in the region of $\aleph(S)$. Then the probability is at most R that $w_0 \geq 1$, where R is defined in Definition 8.

ii. The probability is at most Q_0 that given a $\Theta(n, G, \alpha)$ -sequence S , $\text{Match}(G_L, G_R, S) = \emptyset$.

Proof: Assume that $w_0 \geq 1$. Let w be the number of characters outside of $\aleph(S)$ on the left of M , and let w' be the number of characters outside of $\aleph(S)$ on the right of M . Clearly, $w_0 = w + w'$. Since $w_0 \geq 1$, either $w \geq 1$ or $w' \geq 1$. See Figure 1. Without loss of generality, we assume $w \geq 1$.

Statement i: There are two cases.

Case (a): $1 \leq w < v$. By Lemma 18, the probability for this case is at most $\frac{1}{t}$ for a fixed w . The total probability for this case for $1 \leq w < v$ is at most $\sum_{i=1}^{v-1} \frac{1}{t^i} \leq \sum_{i=1}^{\infty} \frac{1}{t^i} = \frac{1}{t-1}$.

Case (b): $v \leq w$. By Lemma 18, the probability is at most $e^{-\frac{\epsilon^2}{3}w}$ for a fixed w . The total probability for $v \leq w$ is at most $\sum_{w=v}^{\infty} e^{-\frac{\epsilon^2}{3}w} = \frac{e^v}{1-c}$.

The probability analysis is similar when $w' \geq 1$. Therefore, the probability for this case is at most $R = (\frac{1}{t-1} + \frac{e^v}{1-c})$ for $w_0 \geq 1$.

Statement ii: By Lemma 26, with probability at most Q_0 , S does not contain a stable motif region. Therefore, we have probability at most Q_0 that given a random $\Theta(n, G, \alpha)$ -sequence S , $\text{Match}(G_L, G_R, S) = \emptyset$. ■

Lemma 29 shows that we can use G_l and G_r to extract most of the motif regions for the sequences in Z_2 if $G' = G_L$ (recall that G_L is defined right after Lemma 26).

Lemma 29. Assume that G_l and G_r are two sequences of length $d_0 \log n$, and $G_i = \text{Match}(G_l, G_r, S_i'')$ for $S_i'' \in Z_2 = \{S_1'', \dots, S_{k_2}''\}$ and $i = 1, \dots, k_2$ (recall that each sequence G_i is either an empty sequence or a sequence of the length $|G_l|$).

i. If $G_l = G_L$, $G_r = G_R$, and there are no more than yk_2 ($y \in [0, 1]$) sequences S_i'' with $\text{roughLeft}_{S_i''} \notin [\text{LB}(S_i'') - (v + u_2), \text{LB}(S_i'')]$ or $\text{roughRight}_{S_i''} \notin [\text{RB}(S_i''), \text{RB}(S_i'') + (v + u_2)]$, then the probability is at most $e^{-\frac{\epsilon^2 k_2}{3}}$ that there are more than $(Q_0 + y + \epsilon)k_2$ sequences G_i with $G_i = \emptyset$.

ii. For arbitrary G_l and G_r , with probability at most $e^{-\frac{\epsilon^2 k_2}{3}}$, $|\{i | G_i \neq \emptyset \text{ and } G_i \neq \aleph(S_i''), i = 1, \dots, k_2\}| > (R + \epsilon)k_2$, where R is defined in Definition 8.

Proof: Recall that sequence G_{1L} is selected right after Lemma 26.

Statement i: By Lemma 28, for every $S_i'' \in Z_2$, the probability is at most Q_0 that S_i'' does not contain a stable motif region $\aleph(S_i'')$. By Corollary 17, we have probability at most $e^{-\frac{\epsilon^2 k_2}{3}}$ that there are more than $(Q_0 + y + \epsilon)k_2$ sequences G_i with $G_i = \emptyset$.

Statement ii: By Lemma 28, the probability is at most R that $G_i \neq \aleph(S_i'')$. By Corollary 17, with probability at most $e^{-\frac{\epsilon^2 k_2}{3}}$, $|\{i | G_i \neq \aleph(S_i''), i = 1, \dots, k_2\}| > (R + \epsilon)k_2$. ■

Definition 30.

- Given two sequences G_r and G_r , define

$$M(G_r, G_r) = \{G_i'' : G_i'' = \text{Match}(G_l, G_r, \text{roughLeft}_{S_i''}, \text{roughRight}_{S_i''}, S_i'') \mid i = 1, \dots, k_2\}.$$

- For a $\Theta_\alpha(n, G)$ sequence S , define $G_{S,L}$ to be the $\aleph(S)[1, d_0 \log n]$, which is the leftmost subsequence of length $d_0 \log n$ in the motif region of S .
- For a $\Theta_\alpha(n, G)$ sequence S , define $G_{S,R}$ to be the $\aleph(S)[m - d_0 \log n + 1, m]$, which is the rightmost subsequence of length $d_0 \log n$ in the motif region of S , where $m = |G| = |\aleph(S)|$.

the condition iv of Lemma 31

Lemma 31. *Assume that we have the following conditions:*

- For each L with $0 < L \leq \frac{|G|}{2}$, with probability at most $\varsigma_1(n)$, $L_{S_i} \notin [\text{LB}_{S_i} - 2L, \text{LB}_{S_i} + 2L]$ and $R_{S_i} \notin [\text{RB}_{S_i} - 2L, \text{RB}_{S_i} + 2L]$ for $i = 1, 2$, where $(L_{S_1}, R_{S_1}, L_{S_2}, R_{S_2}) = \text{Collision-Detection}(S_1, U_1, S_2, U_2)$, $U_1 = \text{Point-Selection}(S_1, L, [1, |S_1|])$, and $U_2 = \text{Point-Selection}(S_2, L, [1, |S_2|])$.
- For each L with $0 < L \leq \frac{|G|}{2}$, if S_1 has $\text{roughLeft}_{S_1} \notin [\text{LB}_{S_1} - L, \text{LB}_{S_1} + L]$ and $\text{roughRight}_{S_1} \notin [\text{RB}_{S_1} - L, \text{RB}_{S_1} + L]$, then with probability at most $\varsigma_2(n)$, $L_{S_i''} \notin [\text{LB}_{S_i''} - 2L, \text{LB}_{S_i''} + 2L]$ for $i = 1, 2$, where $(L_{S_1}, R_{S_1}, L_{S_i''}, R_{S_i''}) = \text{Collision-Detection}(S_1, U_1, S_i'', U_2)$, $U_1 = \text{Point-Selection}(S_1, L, [\text{roughLeft}_{S_1} - 2L, \text{roughLeft}_{S_1} + 2L]) \cup \text{Point-Selection}(S_1, L, [\text{roughRight}_{S_1} - 2L, \text{roughRight}_{S_1} + 2L])$, and $U_2 = \text{Point-Selection}(S_i'', L, [1, |S_i''|])$.
- The inequality $(P_0 + Q_0) < c_0$ holds for some constant $c_0 < 1$, where Q_0 is defined at equation (13) and $P_0 = \varsigma_1(n) + \frac{2(v+u_1)c^{v+u_1}}{(1-c)^2} + \frac{c^v}{1-c} + \frac{1}{5 \cdot 2^{x_n}}$.
- The inequality $1 - 2(Q_0 + V_0 + (R + 2\epsilon)) - (\alpha + \epsilon) > 0$ holds, where $V_0 = (2(\varsigma_2(n) + (v + u_1)\frac{c^{v+u_2}}{1-c} + \frac{c^v}{1-c}) + \epsilon)$.

Then the algorithm generates a set of at most k_2 subsequences for voting and votes a sequence G' such that

- (1) with probability at most $e^{-\Omega(k_1)} + e^{-\Omega(k_2)}$, $|G'| \neq |G|$, and
- (2) for each $1 \leq i \leq |G|$, with probability at most $e^{-\Omega(k_1)} + e^{-\Omega(k_2)}$, $G'[i] \neq G[i]$.

Before proving Lemma 28, we note that both $\varsigma_1(n)$ and $\varsigma_2(n)$ is at most $\frac{1}{2^{x_n^3}}$ for all of the three algorithms. They will be proved by Lemma 40 and Lemma 41 for the case algorithm-type=RANDOMIZED-SUBLINEAR, Lemma 43 and Lemma 44 for the case algorithm-type=RANDOMIZED-SUBQUADRATIC, and Lemma 47 for the case algorithm-type=DETERMINISTIC-SUPERQUADRATIC.

Proof:

By Lemmas 21, with probability at most $P_0 = \varsigma_1(n) + \frac{2(v+u_1)c^{v+u_1}}{(1-c)^2} + \frac{c^v}{1-c} + \frac{1}{5 \cdot 2^{x_n}}$, $\text{roughLeft}_{S'_{2i-1}} \notin [\text{LB}(S'_{2i-1}) - (v + u_1), \text{LB}(S'_{2i-1})]$ or $\text{roughRight}_{S'_{2i-1}} \notin [\text{RB}(S'_{2i-1}), \text{RB}(S'_{2i-1}) + (v + u_1)]$.

By Lemma 22, with probability at most $P_a = e^{-(0.5-P_0-\epsilon)^2 k_1/3} = e^{\Omega(k_1)}$, the approximate motif length l_{motif} is not in the range $[|G| - 2(v + u_1), |G| + 2(v + u_1)]$.

By Lemma 26, with probability at most Q_0 , a $\Theta_\alpha(n, G)$ sequence does not contain a stable motif region. Therefore, with probability at most $P_1 = (P_0 + Q_0)^{k_1}$, the following statement is false.

- One of S'_{2i-1} for $i = 1, \dots, k_1$ has $\text{roughLeft}_{S'_{2i-1}} \in [\text{LB}(S'_{2i-1}) - (v + u_1), \text{LB}(S'_{2i-1})]$, $\text{roughRight}_{S'_{2i-1}} \in [\text{RB}(S'_{2i-1}), \text{RB}(S'_{2i-1}) + (v + u_1)]$, and has a stable motif region.

By Lemma 25, with probability at most $P_2 = e^{-\frac{\epsilon^2 k_2}{3}}$, there are more than $(2(\varsigma_2(n) + (v + u_1)\frac{c^{v+u_2}}{1-c} + \frac{c^v}{1-c}) + \epsilon)k_2$ sequences S_i'' with $\text{roughLeft}_{S_i''} \notin [\text{LB}(S_i'') - (v + u_2), \text{LB}(S_i'')]$ or

$\text{roughRight}_{S_i''} \notin [\text{RB}(S_i''), \text{LB}(S_i'') + (v + u_2)]$. In other words, with probability at most P_2 , the following statement is false:

(ii) There are no more than $V_0 k_2$ sequences S_i'' with $\text{roughLeft}_{S_i''} \notin [\text{LB}(S_i'') - (v + u_2), \text{LB}(S_i'')]$ or $\text{roughRight}_{S_i''} \notin [\text{RB}(S_i''), \text{RB}(S_i'') + (v + u_2)]$, where $V_0 = (2(\varsigma_2(n) + (v + u_1)\frac{e^{v+u_2}}{1-c} + \frac{e^v}{1-c}) + \epsilon)$.

Assume that Statement (ii) is true. By Lemma 29, with probability at most $P_3 = c^{k_2}$, the following statement is false.

(iii) $M(G_L, G_R)$ contains at most $(Q_0 + V_0 + \epsilon)k_2$ empty sequences.

We start from the rough left boundary roughLeft_1 of S_1 to match the other left boundaries of S_i'' for $i = 1, \dots, k_2$. There are totally at most $2(v + u_1)$ candidates to consider.

By Lemma 29, if $M(G_L, G_r)$, which consists k_2 matched regions, has at most $(Q_0 + V_0 + \epsilon)k_2$ empty sequences, then it has more than $(R + \epsilon)k_2$ from non-motif regions with probability at most $P_4 = 2(v + u_1)e^{-\frac{\epsilon^2 k_2}{3}}$. After the pattern is fixed, those events in the matching are considered to be independent each other. This is why we can apply the Chernoff bound to deal with them. So, the probability is at most P_4 , the following statement is false.

(iv). If $M(G_L, G_r)$ contains at most $(Q_0 + V_0 + \epsilon)k_2$ empty sequences, then $M(G_L, G_r)$ contains at most $(Q_0 + V_0 + \epsilon + (R + \epsilon))k_2 = (Q_0 + V_0 + (R + 2\epsilon))k_2$ elements not from motif regions $\{\mathbb{N}(S_i'') : 1 \leq i \leq k_2\}$.

Therefore, with probability at most $P_1 + P_2 + P_3 + P_4 = e^{-\Omega(k_1)} + e^{-\Omega(k_2)}$, the sequences are not ready for voting in the next phase, which means the following two conditions are satisfied:

(a). There exists G_l and G_r generated by the algorithm such that $M(G_l, G_r)$ contains at most $(Q_0 + V_0 + (R + 2\epsilon))k_2$ elements not from motif regions $\{\mathbb{N}(S_i'') : 1 \leq i \leq k_2\}$.

(b). For every G_l and G_r that $M(G_l, G_r)$ contains at most $(Q_0 + V_0 + \epsilon)k_2$ empty sequences generated by the algorithm, $M(G_l, G_r)$ contains at most $(Q_0 + V_0 + \epsilon + (R + \epsilon))k_2 = (Q_0 + V_0 + (R + 2\epsilon))k_2$ elements not from motif regions $\{\mathbb{N}(S_i'') : 1 \leq i \leq k_2\}$.

Statement (1): For a $M(G_l, G_r)$ with at most $(Q_0 + V_0 + (R + 2\epsilon))k_2$ elements not from motif regions $\{\mathbb{N}(S_i'') : 1 \leq i \leq k_2\}$, we still have $k_2 - (Q_0 + V_0 + (R + 2\epsilon))k_2$ elements in $M(G_l, G_r)$ from motif regions $\{\mathbb{N}(S_i'') : 1 \leq i \leq k_2\}$. By the condition (iv) in this lemma, we have $k_2 - (Q_0 + V_0 + (R + 2\epsilon))k_2 > (Q_0 + V_0 + (R + 2\epsilon))k_2$. Therefore, $|G'|$ is selected to be the length of G in the Voting-Phase().

Statement (2): For a $M(G_l, G_r) = \{G_1'', \dots, G_{k_2}''\}$ with at most $(Q_0 + V_0 + (R + 2\epsilon))k_2$ elements not from motif regions $\{\mathbb{N}(S_i'') : 1 \leq i \leq k_2\}$, we still have $k_2 - (Q_0 + V_0 + (R + 2\epsilon))k_2$ elements in $M(G_l, G_r)$ from motif regions $\{\mathbb{N}(S_i'') : 1 \leq i \leq k_2\}$. By Corollary 17, with probability at most $e^{-\frac{\epsilon^2 k_2}{3}}$ there are more than $(\alpha + \epsilon)k_2$ characters are mutated in the same position among all k_2 the motif regions for the sequences in Z_2 . We have that $k_2 - (Q_0 + V_0 + (R + 2\epsilon))k_2 - (\alpha + \epsilon)k_2 > (Q_0 + V_0 + (R + 2\epsilon))k_2$ by the condition (iv) in this lemma. We let $G'[j]$ be the most frequent character among $G_1''[j], \dots, G_{k_2}''[j]$ in Voting-Phase. Therefore, with probability at most $e^{-\Omega(k_1)} + e^{-\Omega(k_2)}$, $G'[j] \neq G[j]$. ■

We will use multiple variable functions to characterize the computational time for three algorithms. In order to unify the complexity analysis of three algorithm, we introduce the following notation.

Definition 32. A function $T(x, y) : N \times N \rightarrow N$ is monotonic if it is monotonic on both variables. If for arbitrary positive constants c_1 and c_2 , $T(c_1 x, c_2 y) \leq cT(x, y)$ for some positive constant c , then $T(x, y)$ is *slow*.

Lemma 33. Assume that $T(x, y)$, $s(n, L)$ and $g(n, l)$ are monotonic slow functions. Assume that $\text{Collision-Detection}(S_1, U_1, S_2, U_2)$ returns the result in time $t(n, ||U_1|| + ||U_2||)$ time and the $\text{Point-Selection}(S_1, S_2, L)$ selects $s(n, L)$ positions in $g(n, L)$ time. Assume that with probability at most $\varphi(n)$, the function does not stop $\text{Initial-Boundaries}()$ does not stop when $L \leq |G|/4$, and $||U_{S'_{2i-1}}|| + ||U_{S''_j}||$ in the algorithm Recover-Motif is no more than $f(n, |G|)$.

Then with probability at most $k_1\varphi(n)$, the entire algorithm Recover-Motif does not stop in the time complexity $(O(k_1(\sum_{i=1}^{i_0}(T(n, s(n, \frac{n}{2^{i_0 n^{2/5}}})) + g(n, \frac{n}{2^{i_0 n^{2/5}}})) + k_1 h^2 \log n + k_1 k_2 t(n, f(n, |G|)) + h^2 \log n) + k_1 k_2 (\log n)(\log \log n), O(k_2))$, where i_0 is the largest j such that $\frac{n}{2^j n^{2/5}} \leq \min(n^{2/5}, |G|)$ and $h = \min(n^{2/5}, |G|)$.

Proof: The function $\text{Initial-Boundaries}()$ is executed k_1 times. According to the condition that with probability at most $\varphi(n)$, the function does not stop $\text{Initial-Boundaries}()$ does not stop when $L \leq |G|/4$, we have the fact that with probability at most $k_1\varphi(n)$, one of those executions of $\text{Initial-Boundaries}()$ does not stop when $L \leq |G|/4$.

In the rest of the proof, we assume that all executions of $\text{Initial-Boundaries}()$ stops when $L \leq |G|/4$.

When $L = O(h)$, we detect rough left and right motif boundaries and run $\text{Improve-Boundaries}()$, which takes $O(h^2 \log n)$ time. It takes $O(\sum_{i=1}^{i_0}(T(n, s(n, \frac{n}{2^{i_0 n^{2/5}}})) + g(n, \frac{n}{2^{i_0 n^{2/5}}})) + h^2 \log n)$ time to run $\text{Initial-Boundaries}(S'_{2i-1}, S'_{2i})$ one time for one pair (S'_{2i-1}, S'_{2i}) in Z_1 . It takes $O(k_1(\sum_{i=1}^{i_0}(t(n, s(n, \frac{n}{2^{i_0 n^{2/5}}})) + g(n, \frac{n}{2^{i_0 n^{2/5}}})) + k_1 h^2 \log n)$ time to run $\text{Initial-Boundaries}(S'_{2i-1}, S'_{2i})$ one time for all pairs (S'_{2i-1}, S'_{2i}) in Z_1 .

It takes $k_2(t(n, f(n, |G|)) + h^2 \log n)$ time to find the rough boundaries for all sequences in Z_2 with a fixed sequence S from Z_1 by executing the for loop “For each $S''_j \in Z_2$ ” in the algorithm Recover-Motif . It takes $k_1 k_2(t(n, f(n, |G|)) + h^2 \log n)$ time to find the rough boundaries for all sequences in Z_2 via all sequences S'_{2i-1} from Z_1 through for loop “For each $S''_j \in Z_2$ ” in the algorithm Recover-Motif .

Recall that parameters v and u_1 are constants, and u_2 is $O(\log \log n)$. Calling $\text{Match}(G_l, G_r, S''_i)$ takes $O((v + u_2) \log n)$ time for each $S''_i \in Z_2$. The total times for calling $\text{Match}(G_l, G_r, S''_i)$ is $O(k_1 k_2 (v + u_1)(v + u_2) \log n) = O(k_1 k_2 (\log n)(\log \log n))$.

The voting part takes $O(k_2)$ time for executing voting for recovering one character in motif. ■

5.4. Randomized Algorithms for Motif Detection

In this section, we present two randomized algorithms for motif detection. The first one is a sublinear time algorithm that can handle $\frac{1}{(\log n)^{2+\mu}}$ mutation, and the second one is a super-linear time algorithm that can handle $\Omega(1)$ mutation. They also share some common functions.

Lemma 34. Let c be a constant in $(0, 1)$. Assume m and n are two non-negative integer with $m \leq n$. Then for every integer m_1 with $0 \leq m_1 \leq \frac{\delta_c m}{\ln n}$, $\binom{n}{m_1} c^m \leq e^{(m \ln c)/2}$, where constant $\delta_c = \frac{-\ln c}{2}$ as defined in Definition 8.

Proof: We have the inequalities

$$\binom{n}{m_1} c^m \leq n^{m_1} c^m \quad (33)$$

$$= e^{m_1 \ln n} c^m \quad (34)$$

$$\leq e^{\frac{\delta_c m}{\ln n} \ln n} c^m \quad (35)$$

$$= e^{\delta_c m} e^{m \ln c} \quad (36)$$

$$= e^{(m \ln c)/2} \quad (37)$$

■

Lemma 35. *Let $S = U \cup V$ be a set of n elements with $U \cap V = \emptyset$. Assume that x_1, \dots, x_m are m random elements in S . Then with probability at most $\binom{\|U\|}{m_1} (\frac{\|V\|+m_1}{n})^m$, the list x_1, \dots, x_m contains at most m_1 different elements from U (in other words, $|\{x_1, \dots, x_m\} \cap U| \leq m_1$).*

Proof: For a subset $S' \subseteq S$ with $|S'| = m_1$, the probability is at most $(\frac{m_1}{n})^m$ that all elements x_1, \dots, x_m are in S' . For every subset $X \subseteq S$ with $|X| \leq m_1$, there exists another subset $S' \subseteq S$ such that $|S'| = m_1$. We have that $\Pr[|\{x_1, \dots, x_m\} \cap U| \leq m_1] \leq \Pr[\{x_1, \dots, x_m\} \cap U \subseteq U' \text{ for some } U' \subseteq U \text{ with } \|U'\| = m_1]$. There are $\binom{\|U\|}{m_1}$ subsets of U with size m_1 . We have the probability at most $\binom{\|U\|}{m_1} (\frac{\|V\|+m_1}{n})^m$ that x_1, \dots, x_m contains at most m_1 different elements in U . ■

Lemma 36. *Let δ be the same as that in Lemma 34. Let β be a constant in $(0, 1)$ and $c = 1 - \frac{\beta}{2}$. Let $m_1 \leq \frac{\delta_c m}{\ln \beta n}$ and $m \leq n^{1-\epsilon}$ for some fixed $\epsilon > 0$. Let S_1 and S_2 be two sets of n elements with $|S_1 \cap S_2| \geq \beta n$ and C be a set of size $|C| \leq \gamma m_1$ for some constant $\gamma \in (0, 1)$. Then for all large n , with probability is at most $2e^{-\frac{(1-\gamma)m_1 m}{n}}$, we have $(A - C) \cap (B - C) = \emptyset$, where $A = \{x_1, \dots, x_m\}$ and $B = \{y_1, \dots, y_m\}$ are two sets, which may have multiplicities, of m random elements from S_1 and S_2 , respectively.*

Proof: In the entire proof of this lemma, we always assume that n is sufficiently large. We are going to give an upper bound about the probability that B does not contain any element in $A - C$. For each element $y_i \in B$, with probability at most $1 - \frac{m_1}{n}$ that y_i is not in A . Therefore, the probability is at most $(1 - \frac{\|A\| - \|C\|}{n})^m$ that B does not contain any element in $A - C$.

By Lemma 35, the probability is at most $\binom{\beta n}{m_1} (\frac{(1-\beta)n+m_1}{n})^m$ that $\|A \cap (S_1 \cap S_2)\| \leq m_1$. We have the inequalities

$$\Pr[(A - C) \cap (B - C) = \emptyset] \quad (38)$$

$$= \Pr[(A - C) \cap (B - C) = \emptyset \mid \|A \cap (S_1 \cap S_2)\| \geq m_1] \cdot \Pr[\|A \cap (S_1 \cap S_2)\| \geq m_1] + \quad (39)$$

$$\Pr[(A - C) \cap (B - C) = \emptyset \mid \|A \cap (S_1 \cap S_2)\| < m_1] \cdot \Pr[\|A \cap (S_1 \cap S_2)\| < m_1] \quad (40)$$

$$\leq \Pr[(A - C) \cap (B - C) = \emptyset \mid \|A \cap (S_1 \cap S_2)\| \geq m_1] + \Pr[\|A \cap (S_1 \cap S_2)\| < m_1] \quad (41)$$

$$\leq (1 - \frac{\|(A \cap S_1 \cap S_2)\| - \|C\|}{n})^m + \binom{\beta n}{m_1} (\frac{(1-\beta)n+m_1}{n})^m \quad (42)$$

$$\leq (1 - \frac{(1-\gamma)m_1}{n})^m + \binom{\beta n}{m_1} (\frac{(1-\beta)n+m_1}{n})^m \quad (43)$$

$$\leq e^{-\frac{(1-\gamma)m_1 m}{n}} + \binom{\beta n}{m_1} (\frac{(1-\beta)n+m_1}{n})^m \quad (44)$$

$$\leq e^{-\frac{(1-\gamma)m_1 m}{n}} + \binom{\beta n}{m_1} (1 - \frac{\beta}{2})^m \quad (45)$$

$$\leq e^{-\frac{(1-\gamma)m_1 m}{n}} + e^{(m \ln c)/2} \quad (46)$$

$$\leq 2e^{-\frac{(1-\gamma)m_1 m}{n}}. \quad (47)$$

The inequality $(1 - \frac{(1-\gamma)m_1}{n})^m \leq e^{-\frac{(1-\gamma)m_1 m}{n}}$, which is used from (43) to (44), follows from the fact that $1 - x \leq e^{-x}$. The transition from (44) to (45) follows from the fact $\frac{m_1}{n} \leq \frac{\beta}{2}$ since $m_1 = o(n)$ according to the conditions of the lemma.

It is easy to see that $\frac{2(1-\gamma)m_1 m}{-m \ln c} = \frac{2(1-\gamma)m_1}{-\ln c} \leq n$ for all large n . Thus, $\frac{(1-\gamma)m_1 m}{n} \geq (m \ln c)/2$ (note that $\ln c < 0$ as $c \in (0, 1)$). Thus, by Lemma 34, $\binom{\beta n}{m_1} (1 - \frac{\beta}{2})^m \leq e^{m \ln c/2} \leq e^{-\frac{(1-\gamma)m_1 m}{n}}$. This is why we have the transition from (46) to (47). Therefore, $\Pr[(A-C) \cap (B-C) = \emptyset] \leq 2e^{-\frac{(1-\gamma)m_1 m}{n}}$. \blacksquare

5.4.1. Sublinear Time Algorithm for $\frac{1}{(\log n)^{2+\mu}}$ Mutation Rate

In this section, we give an algorithm for the case with at most $\frac{1}{(\log n)^{2+\mu}}$ mutation rate. The performance of the algorithm is stated in Theorem 2.

Definition 37. A position p in the motif region $\aleph(S)$ of an input sequence S is *damaged* if there exists at least one mutation in $S[p, p + d_0 \log n - 1]$.

Lemma 38. Assume that $\alpha L = (\log n)^{1+\Omega(1)}$. With probability at most $e^{-(\log n)^{1+\Omega(1)}}$, there are more than $\frac{M_1}{(\log n)^{\Omega(1)}}$ positions that are from the M sampled positions in an interval of length L and are damaged.

Proof: By Theorem 16, with probability at most $P_1 = 2^{-\alpha L}$ (let $\delta = 2$), there are more than $3\alpha L$ mutation in an interval of length L . Therefore, with probability at most $2^{-\alpha L} = e^{-(\log n)^{1+\Omega(1)}}$, there are more than $3\alpha L \log n$ positions are damaged. Therefore, each random position in an interval of length L has at most probability $\frac{3\alpha L \log n}{L} = 3\alpha \log n$ to be damaged.

Since $\alpha = (\frac{1}{(\log n)^{2+\Omega(1)}})$ and M positions are sampled, by Theorem 16, with probability at most $P_2 = 2^{-(3\alpha \log n)M} = e^{-(\log n)^{1+\Omega(1)}}$ (let $\delta = 2$), the number of damaged positions sampled in an interval of length L is more than $(1 + \delta)3\alpha \log n M = (9\alpha \log n)M = \frac{M_1}{(\log n)^{\Omega(1)}}$. Thus, with total probability at most $P_1 + P_2 = e^{-(\log n)^{1+\Omega(1)}}$, there are more than $\frac{M_1}{(\log n)^{\Omega(1)}}$ damaged positions that are from the M sampled positions in an interval of length L . \blacksquare

Definition 39. Let A be a set of positions in an input sequence S with $\aleph(S) = [i, j]$. Let $A(S, \aleph(S)) = A \cap [i, j]$.

Lemma 40. Assume that $|G| \geq \frac{(\log n)^{3+\tau}}{100}$ and $d_0 \log n \leq L \leq |G|/2$. Let I_1 be a union of intervals that include $[\text{LB}(S_1) - 2L, \text{LB}(S_1) + 2L]$ and $[\text{RB}(S_1) - 2L, \text{RB}(S_1) + 2L]$. Let $U_1 = \text{Point-Selection}(S_1, L, I_1)$, $U_2 = \text{Point-Selection}(S_2, L, [1, |S_2|])$, and $(L_{S_1}, R_{S_1}, L_{S_2}, R_{S_2}) = \text{Collision-Detection}(S_1, U_1, S_2, U_2)$. Then

- i. With probability at most $\frac{1}{2^{x n^3}}$, the left rough boundary L_{S_1} has at most $2L$ distance from $\text{LB}(S_1)$ and the left rough boundary L_{S_2} has at most $2L$ distance from $\text{LB}(S_2)$.
- ii. With probability at most $\frac{1}{2^{x n^3}}$, the right rough boundary R_{S_1} has at most $2L$ distance from $\text{RB}(S_1)$; and the right boundary of R_{S_2} has at most $2L$ distance from $\text{RB}(S_2)$.

Proof: We prove the following two statements which imply the lemma.

- i. With probability at most $\frac{1}{2^x n^3}$, there is no intervals A_i from S_1 and B_j from S_2 such that (1) $|A_i(S_1, \aleph(S_1)) \cap B_j(S_2, \aleph(S_2))|$ is at least $\frac{L}{2}$; (2) the left boundary of S_1 has at most $2L$ distance from A_i ; (3) the left boundary of S_2 has at most $2L$ distance from B_j ; and (4) there is collision between the sampled positions in A_i and B_j .
- ii. With probability at most $\frac{1}{2^x n^3}$, there is no intervals A_i from S_1 and B_j from S_2 such that (1) $|A_i(S_1, \aleph(S_1)) \cap B_j(S_2, \aleph(S_2))|$ is at least $\frac{L}{2}$; (2) the right boundary of S_1 has at most $2L$ distance from A_i ; (3) the right boundary of S_2 has at most $2L$ distance from B_j ; and (4) there is collision between the sampled positions in A_i and B_j .

We only prove the statement i. The proof for statement ii is similar to that for statement i. Note that L goes down by half each cycle in the algorithm. Assume that L satisfies the condition of this lemma.

Select A_i from S_1 and B_j from S_2 to be the first pair of intervals with $||A_i(S_1, \aleph(S_1)) \cap B_j(S_2, \aleph(S_2))|| \geq \frac{L}{2}$. It is easy to see that such a pair exists and both have distance from the left boundary with distance at most $2L$. This is because when an leftmost interval of length L is fully inside the motif region of the first sequence, we can always find the second interval from the second sequence with intersection of length at least $\frac{L}{2}$.

Replace m by $M(L)$, m_1 by $M_1(L)$ (see Definition 10), and n by L to apply Lemma 36. We also let C be the set of damaged positions affected by the mutated positions. With probability at most $o(\frac{1}{2^x n^3})$, C has size more than $\Omega(M_1(L))$ by Lemma 38. With probability at most $o(\frac{1}{2^x n^3})$, there is an no intersection A_i from S_1 and B_j from S_2 . \blacksquare

Lemma 41. Assume that $|G| < \frac{(\log n)^{3+\tau}}{100}$ and L is an integer with $d_0 \log n \leq L \leq |G|/2$. Let I_1 be a union of intervals that include $[\text{LB}(S_1) - 2L, \text{LB}(S_1) + 2L]$ and $[\text{RB}(S_1) - 2L, \text{RB}(S_1) + 2L]$. Let $U_1 = \text{Point-Selection}(S_1, L, I_1)$, $U_2 = \text{Point-Selection}(S_2, L, [1, |S_2|])$, and $(L_{S_1}, R_{S_1}, L_{S_2}, R_{S_2}) = \text{Collision-Detection}(S_1, U_1, S_2, U_2)$. Then

- i. With probability at most $\frac{1}{2^x n^3}$, the left rough boundary L_{S_1} has at most $|G|/4$ distance from $\text{LB}(S_1)$ and the left rough boundary L_{S_2} has at most $|G|/4$ distance from $\text{LB}(S_2)$.
- ii. With probability at most $\frac{1}{2^x n^3}$, the right rough boundary R_{S_1} has at most $|G|/4$ distance from $\text{RB}(S_1)$; and the right boundary of R_{S_2} has at most $|G|/4$ distance from $\text{RB}(S_2)$.

Proof: For two sequences S_1 and S_2 , it is easy to see that there a common position in both motif regions of the two sequences such that there is no mutation in the next $d_0 \log n$ characters with high probability. This is because that mutation probability is small.

By Theorem 16, with probability at most $P_{l,1} = 2^{-\alpha|G|/4}$ (let $\delta = 2$), there are more than $3\alpha \frac{|G|}{4}$ mutated characters in the interval $\aleph(S_i)[1, \frac{|G|}{4}]$ for $i = 1, 2$. Therefore, with probability at most $2^{-\alpha|G|/4} = e^{-(\log n)^{1+\Omega(1)}}$, there are more than $3\alpha \frac{|G|}{4} \log n$ positions are damaged in $\aleph(S_i)[1, \frac{|G|}{4}]$.

Since the mutation probability is $\alpha = (\frac{1}{(\log n)^{2+\Omega(1)}})$ and $M(L)$ positions are sampled, with probability at most $P_{l,2} = 2^{-(3\alpha d_0 \log n) \frac{|G|}{4}} = e^{-(\log n)^{1+\Omega(1)}}$ (with $\delta = 2$), the number of damaged positions is more than $((5\alpha d_0 \log n) \frac{|G|}{4}) = \frac{|G|}{(\log n)^{\Omega(1)}}$ by Theorem 16. The probability is $P_l = P_{l,1} + P_{l,2} = e^{-(\log n)^{1+\Omega(1)}}$ that left side has more than $((5\alpha d_0 \log n) \frac{|G|}{4}) = \frac{|G|}{(\log n)^{\Omega(1)}}$ damaged positions.

We have similar $P_r = P_{r,1} + P_{r,2} = e^{-(\log n)^{1+\Omega(1)}}$ probability for the right side for more than $((5\alpha d_0 \log n) \frac{|G|}{4}) = \frac{|G|}{(\log n)^{\Omega(1)}}$ damaged positions in $\aleph(S_i)[\frac{3|G|}{4} - 1, |G|]$.

Now we assume that left side has more than $((5\alpha d_0 \log n) \frac{|G|}{4}) = \frac{|G|}{(\log n)^{\Omega(1)}}$ damaged positions and the right side for more than $((5\alpha d_0 \log n) \frac{|G|}{4}) = \frac{|G|}{(\log n)^{\Omega(1)}}$ damaged positions in $\aleph(S_i)[\frac{3|G|}{4} - 1, |G|]$. Since each position in each interval of length L is selected in $\text{Point-Selection}(S_1, S_2, L)$???, it is easy to verify the conclusions of this lemma. \blacksquare

Lemma 42. *For the case algorithm-type=RANDOMIZED-SUBLINEAR, we have*

- i. *CollisionDetection(S_1, U_1, S_2, U_2) takes $t(n, ||U_1|| + ||U_2||) = O((||U_1|| + ||U_2||) \log n)$ time.*
- ii. *Point-Selection($S_1, L, [1, |S_1|]$) selects $s(n, L) = O((\frac{n}{L})M(L))$ positions in $g(n, L) = O(s(n, L))$ time if $L \geq \frac{(\log n)^{3+\tau}}{100}$.*
- iii. *Point-Selection($S_1, L, [1, |S_1|]$) selects $s(n, L) = O(n)$ positions in $g(n, L) = O(n)$ time if $L < \frac{(\log n)^{3+\tau}}{100}$.*
- iv. *$||U_{S'_{2i-1}}|| + ||U_{S'_j}||$ in the algorithm Recover-Motif is no more than $f(n, |G|) = O(M(|G|) + \frac{n}{|G|}M(|G|))$.*
- v. *With probability at most $\frac{k}{2^x n^3}$, the algorithm Recover-Motif does not stop in $(O(k(\frac{n}{\sqrt{h}}(\log n)^{\frac{5}{2}} + h^2 \log n)), O(k))$ time.*

Proof: Statement i. The parameter $\omega_{\text{RANDOMIZED-SUBLINEAR}}$ is set to be 0 in the Collision-Detection. It follows from the time complexity of bucket sorting, which is described in standard algorithm textbooks.

Statements ii and iii. They follows from the implementation of $\text{Point-Selection}()$.

Statement iv. It follows from the choice of $\text{Point-Selection}()$ for the sublinear time algorithm at Recover-Motif().

Statement v. It follows from Lemma 41, Lemma 40, Lemma 33 and Statements i, ii, and iii, and iv. \blacksquare

We give the proof for Theorem 2.

Proof: [Theorem 2] The computational time part of this theorem follows from Lemma 42.

By Lemma 40, Lemma 41, we can let $\varsigma_1(n) = \frac{1}{2^x n^3} \leq \varsigma_0$ for the probability bound $\varsigma_1(n)$ in the condition (i) of Lemma 31.

By Lemma 40, Lemma 41, we can let $\varsigma_2(n) = \frac{1}{2^x n^3} \leq \varsigma_0$ for the probability bound $\varsigma_1(n)$ in the condition (ii) of Lemma 31.

By inequality (12), the condition (iii) of Lemma 31 is satisfied.

By inequality (11), we know that the condition (iv) of Lemma 31 can be satisfied.

The failure probability part of this theorem follows from Lemma 20, and Lemma 31 by using the fact that k_1, k_2 , and k are of the same order (see equation (18)). \blacksquare

5.4.2. Randomized Algorithm for $\Omega(1)$ Mutation Rate

In this section, we give an algorithm for the case with $\Omega(1)$ mutation rate. The performance of the algorithm is stated in Theorem 4.

Lemma 43. *Assume that $d_0 \log n \leq L \leq |G|/2$ and $|G| \geq \frac{(\log n)^{3+\tau}}{100}$. Let I_1 be a union of intervals that include $[\text{LB}(S_1) - 2L, \text{LB}(S_1) + 2L]$ and $[\text{RB}(S_1) - 2L, \text{RB}(S_1) + 2L]$. Let $U_1 = \text{Point-Selection}(S_1, L, I_1)$, $U_2 = \text{Point-Selection}(S_2, L, [1, |S_2|])$, and $(L_{S_1}, R_{S_1}, L_{S_2}, R_{S_2}) = \text{Collision-Detection}(S_1, U_1, S_2, U_2)$. Then*

- i. With probability at most $\frac{1}{2^{xn^3}}$, the left rough boundary L_{S_1} has at most $2L$ distance from $LB(S_1)$ and the left rough boundary L_{S_2} has at most $2L$ distance from $LB(S_2)$.
- ii. With probability at most $\frac{1}{2^{xn^3}}$, the right rough boundary R_{S_1} has at most $2L$ distance from $RB(S_1)$; and the right boundary of R_{S_2} has at most $2L$ distance from $RB(S_2)$.

Proof: We prove the following two statements which imply the lemma.

- i. With probability at most $\frac{1}{2^{xn^3}}$, there is no intervals A_i from S_1 and B_j from S_2 such that (1) $\|A_i(S_1, \aleph(S_1)) \cap B_j(S_2, \aleph(S_2))\|$ is at least $\frac{L}{2}$; (2) The left boundary of S_1 has at most $2L$ distance from A_i ; (3) The left boundary of S_2 has at most $2L$ distance from B_j ; and (4) There is collision between the sampled positions in A_i and B_j .
- ii. With probability at most $\frac{1}{2^{xn^3}}$, there is no intervals A_i from S_1 and B_j from S_2 such that (1) $\|A_i(S_1, \aleph(S_1)) \cap B_j(S_2, \aleph(S_2))\|$ is at least $\frac{L}{2}$; (2) The right boundary of S_1 has at most $2L$ distance from A_i ; (3) The right boundary of S_2 has at most $2L$ distance from B_j ; and (4) There is collision between the sampled positions in A_i and B_j .

We only prove the statement i. The proof for statement ii is similar. Note that L goes down by half each cycle in the algorithm. Assume that L_0 satisfies the condition of this lemma, and let $L = L_0$ happen in the algorithm.

Select A_i from S_1 and B_j from S_2 to be the first pair of intervals with $\|A_i(S_1, \aleph(S_1)) \cap B_j(S_2, \aleph(S_2))\| \geq \frac{L}{2}$. It is easy to see that such a pair exists and both have distance from the left boundary with distance at most $2L$. This is because when an leftmost interval of length L is fully inside the motif region of the first sequence, we can always find the second interval from the second sequence with intersection of length at least $\frac{L}{2}$.

Replace m by $M(L)$, m_1 by $M_1(L)$ (see Definition 10), and n by L to apply Lemma 36. We do not consider any damaged position in this algorithm, therefore, let C be empty. With probability at most $o(\frac{1}{2^{xn^3}})$, there is no intersection A_i from S_1 and B_j from S_2 . \blacksquare

Lemma 44. Let U_1 and U_2 contain all positions of the input sequences S_1 and S_2 , respectively. Assume $(L_{S_1}, R_{S_1}, L_{S_2}, R_{S_2}) = \text{Collision-Detection}(S_1, U_1, S_2, U_2)$. Then

- i. With probability at most $\frac{1}{2^{xn^3}}$, the left rough boundary L_{S_1} has at most $d_0 \log n$ distance from $LB(S_1)$ and the left rough boundary L_{S_2} has at most $d_0 \log n$ distance from $LB(S_2)$.
- ii. With probability at most $\frac{1}{2^{xn^3}}$, the right rough boundary R_{S_1} has at most $d_0 \log n$ distance from $RB(S_1)$; and the right rough boundary of R_{S_2} has at most $d_0 \log n$ distance from $RB(S_2)$.

Proof: For two sequences S_1 and S_2 , let $\aleph(S_a)$ be the subsequence $S_a[i_a, j_a]$ for $a = 1, 2$. By Corollary 17, with probability at most $P_l = 2c^{d_0 \log n} \leq \frac{2}{5 \cdot 2^{xn^3}}$ (see inequality 8 at Definition 14), there are more than $(\alpha + \epsilon)d_0 \log n$ mutations in $S_a[i_a, i_a + d_0 \log n - 1]$ for $a = 1, 2$.

In this case, every position in the two sequences S_1 and S_2 is selected by Point-Selection(S_1, S_2). With probability at most P_l , the left boundary position is missed during the matching. We have similar P_r to miss the right boundary.

Assume that p_1 and p_2 are two positions of S_1 and S_2 respectively. If one of two positions is outside the motif region and has more than $d_0 \log n$ distance to the motif boundary, with probability at most $c^{-d_0 \log n} \leq \frac{1}{5 \cdot 2^{xn^3}}$ (see inequality 8 at Definition 14) for them to match that requires $\text{diff}(Y_1, Y_2) \leq \beta$ by Lemma 18, where Y_a is a subsequence $S_a[p_a, p_a + d_0 \log n - 1]$ for $a = 1, 2$. \blacksquare

Lemma 45. Assume that $d_0 \log n \leq L \leq |G|/2$ and $c_0 \log n \leq |G| < \frac{(\log n)^{3+\tau}}{100}$. Let I_1 be a union of intervals that include $[\text{LB}(S_1) - 2L, \text{LB}(S_1) + 2L]$ and $[\text{RB}(S_1) - 2L, \text{RB}(S_1) + 2L]$. Let $U_1 = \text{Point-Selection}(S_1, L, I_1)$, $U_2 = \text{Point-Selection}(S_2, L, [1, |S_2|])$, and $(L_{S_1}, R_{S_1}, L_{S_2}, R_{S_2}) = \text{Collision-Detection}(S_1, U_1, S_2, U_2)$. Then

- i. With probability at most $\frac{1}{2^{x n^3}}$, the left rough boundary L_{S_1} has at most $d_0 \log n$ distance from $\text{LB}(S_1)$ and the left rough boundary L_{S_2} has at most $d_0 \log n$ distance from $\text{LB}(S_2)$.
- ii. With probability at most $\frac{1}{2^{x n^3}}$, the right rough boundary R_{S_1} has at most $d_0 \log n$ distance from $\text{RB}(S_1)$; and the right boundary of R_{S_2} has at most $d_0 \log n$ distance from $\text{RB}(S_2)$.

Proof: In this case, every position in the two sequences S_1 and S_2 is selected by Point-Selection(S_1, S_2). It follows from Lemma 44. ■

Lemma 46. For the case algorithm-type=RANDOMIZED-SUBQUADRATIC, we have

- i. $\text{CollisionDetection}(S_1, U_1, S_2, U_2)$ takes $t(n, ||U_1|| + ||U_2||) = O((||U_1|| + ||U_2||)^2 \log n)$ time.
- ii. $\text{Point-Selection}(S_1, L, [1, |S_1|])$ selects $s(n, L) = O((\frac{n}{L})M(L))$ positions in $g(n, L) = O(s(n, L))$ time if $L \geq \frac{(\log n)^{3+\tau}}{100}$.
- iii. $\text{Point-Selection}(S_1, L, [1, |S_1|])$ selects $s(n, L) = O(n)$ positions in $g(n, L) = O(n)$ time if $L < \frac{(\log n)^{3+\tau}}{100}$.
- iv. $||U_{S'_{2i-1}}|| + ||U_{S'_j}||$ in the algorithm Recover-Motif is no more than $f(n, |G|) = O(M(|G|) + \frac{n}{|G|}M(|G|))$.
- v. With probability at most $\frac{k}{2^{x n^3}}$, the algorithm Recover-Motif does not stop in $(O(k(\frac{n^2}{|G|}(\log n)^{O(1)} + h^2 \log n)), O(k))$ time.

Proof: Statement i. The parameter $\omega_{\text{RANDOMIZED-SUBLINEAR}}$ is set to be β in the Collision-Detection. It follows from the time complexity of brute force method.

Statements ii and iii. They follows from the implementation of Point-Selection().

Statement iv. It follows from the choice of Point-Selection(.) for the sublinear time algorithm at Recover-Motif().

Statement v. It follows from Lemma 44, Lemma 45, Lemma 33, and Statements i, ii, and iii. ■

We give the proof for Theorem 6.

Proof: [Theorem 4] The computational time part of this theorem follows from Lemma 46.

By Lemma 43, Lemma 44, we can let $\varsigma_1(n) = \frac{1}{2^{x n^3}} \leq \varsigma_0$ for the probability bound $\varsigma_1(n)$ in the condition (i) of Lemma 31.

By Lemma 43, Lemma 44, we can let $\varsigma_2(n) = \frac{1}{2^{x n^3}} \leq \varsigma_0$ for the probability bound $\varsigma_2(n)$ in the condition (i) of Lemma 31.

By inequality (12), the condition (iii) of Lemma 31 is satisfied.

By inequality (11), we know that the condition (iv) of Lemma 31 can be satisfied.

The failure probability part of this theorem follows from Lemma 20, and Lemma 31 by using the fact that k_1, k_2 , and k are of the same order (see equation (18)). ■

5.5. Deterministic Algorithm for $\Omega(1)$ Mutation Rate

In this section, we give a deterministic algorithm for the case with $\Omega(1)$ mutation rate. The performance of the algorithm is stated in Theorem 6.

Lemma 47. *Assume that $d_0 \log n \leq L \leq |G|/2$ and $c_0 \log n \leq |G|$. Let I_1 be a union of intervals that include $[\text{LB}(S_1) - 2L, \text{LB}(S_1) + 2L]$ and $[\text{RB}(S_1) - 2L, \text{RB}(S_1) + 2L]$. Let $U_1 = \text{Point-Selection}(S_1, L, I_1)$, $U_2 = \text{Point-Selection}(S_2, L, [1, |S_2|])$, and $(L_{S_1}, R_{S_1}, L_{S_2}, R_{S_2}) = \text{Collision-Detection}(S_1, U_1, S_2, U_2)$. Then*

- i. *With probability at most $\frac{1}{2^{x_n^3}}$, the left rough boundary L_{S_1} has at most $d_0 \log n$ distance from $\text{LB}(S_1)$ and the left rough boundary L_{S_2} has at most $d_0 \log n$ distance from $\text{LB}(S_2)$.*
- ii. *With probability at most $\frac{1}{2^{x_n^3}}$, the right rough boundary R_{S_1} has at most $d_0 \log n$ distance from $\text{RB}(S_1)$; and the right rough boundary of R_{S_2} has at most $d_0 \log n$ distance from $\text{RB}(S_2)$.*

Proof: In this case, every position in the two sequences S_1 and S_2 is selected by Point-Selection(S_1, S_2). It follows from Lemma 44. ■

Lemma 48. *For the case algorithm-type=DETERMINISTIC-SUPERQUADRATIC, we have*

- i. *CollisionDetection(S_1, U_1, S_2, U_2) takes $t(n, ||U_1|| + ||U_2||) = O((||U_1|| + ||U_2||)^2 \log n)$ time.*
- ii. *Point-Selection($S_1, L, [1, |S_1|]$) selects $s(n, L) = O(n)$ positions in $g(n, L) = O(n)$ time.*
- iii. *$||U_{S'_{2i-1}}|| + ||U_{S'_j}||$ in the algorithm Recover-Motif is no more than $f(n, |G|) = O(|G| + n)$.*
- iv. *With probability at most $\frac{k}{2^{x_n^3}}$, the algorithm Recover-Motif does not stop ($O(k(n^2(\log n)^{O(1)} + h^2 \log n), O(k))$).*

Proof: Statement i. The parameter $\omega_{\text{DETERMINISTIC-SUPERQUADRATIC}}$ is set to be β in the Collision-Detection. It follows from the time complexity of brute force method.

Statement ii. They follows from the implementation of Point-Selection().

Statement iii. It follows from the choice of Point-Selection(.) for the sublinear time algorithm at Recover-Motif().

Statement iv. It follows from Lemma 47, Lemma 33 and Statements i, ii, and iii. ■

We give the proof for Theorem 6.

Proof: [Theorem 6] The computational time part of this theorem follows from Lemma 48.

By Lemma 47, we let $\varsigma_1(n) = \frac{1}{2^{x_n^3}} \leq \varsigma_0$ for the probability bound $\varsigma_1(n)$ in the condition (i) of Lemma 31.

By Lemma 47, we can let $\varsigma_2(n) = \frac{1}{2^{x_n^3}} \leq \varsigma_0$ for the probability bound $\varsigma_2(n)$ in the condition (i) of Lemma 31.

By inequality (12), the condition (iii) of Lemma 31 is satisfied.

By inequality (11), we know that the condition (iv) of Lemma 31 can be satisfied.

The failure probability part of this theorem follows from Lemma 20, and Lemma 31 by using the fact that k_1, k_2 , and k are of the same order (see equation (18)). ■

6. Conclusions

We develop an algorithm that under the probabilistic model. It finds the implanted motif with high probability if the alphabet size is at least 4, the motif length is in $[(\log n)^{7+\mu}, \frac{n}{(\log n)^{1+\mu}}]$ and each character in motif region has probability at most $\frac{1}{(\log n)^{2+\mu}}$ of mutation. The motif region can be detected and each motif character can be recovered in sublinear time. A sub-quadratic randomized algorithm is developed to recover the motif with $\Omega(1)$ mutation rate. A quadratic deterministic algorithm is developed to recover the motif with $\Omega(1)$ mutation rate. It is interesting problem if there is an algorithm to handle the case for the alphabet of size 3. A more interesting problem is to extend the algorithm to handle larger mutation probability.

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7. Experimental Results

7.1. Implementation and Results

Aiming at solving the motif discovery problem, we implemented our algorithm by JAVA. Our program could accept many popular DNA sequence data formats, such as FASTA, GCG, GenBank and so on. Our tests were all done on a PC with an Intel Core 1.5G CPU and 3.0G Memory.

In the first experiment, we tested our algorithm on several sets of simulated data, which are all generated from our probability model with a small mutation rate. All input sets contain 20 or 15 sequences, each of length is 600 or 500 base pair. And each bp of all the simulated gene sequences was generated independently with the same occurrence probability. A motif with a length of 15 or 12 was randomly planted to each input sequence. The number of iterations is between 10 and 30. The minimum Hamming distances between the results and consensus are recorded.

	N	M	L	R	Accuracy	timecost
Sets1	20	600	15	10	100	23
Sets1	20	600	15	30	100	85
Sets2	15	600	15	10	95	18
Sets3	20	600	12	10	95	15
Sets4	20	500	15	20	100	112

Tab 1. Results on simulated data

In the second experiment, we tested our algorithm on real sets of sequences, which are obtained from SCPD. SCPD contains a large number of gene data and transcription factors of yeast. For each set of gene sequences that are regulated by the same motif, we chose 1000bp as the length of input gene sequence. In order to make comparisons among several existed motif finding methods, we also tested Gibbs, MEME, Info-Gibbs and Consensus in our experiment to show the difference of their performance. Here are the specific experimental results:

	Number of Sequences	Motif Length
GCR1	6	10

Tab 2. Number of sequences and motif length

	GCR1
Voting	4
Gibbs	5
MEME	10
InfoGibbs	5
Consensus	5

Tab 3. Total number of mismatch positions compared to motif

	GCR1
Voting	0.67
Gibbs	0.83
MEME	1.67
InfoGibbs	0.83
Consensus	0.83

Tab 4. Average mismatch numbers per sequence

7.2. Analysis

In the first experiment, we tested our algorithm on 4 sets of simulated sequences. From our experimental results, we find that the accuracy of our algorithm for finding motif in simulated data is nearly 100%. The accuracies of the experiments in simulated data sets are satisfactory. Our algorithm can get the results within several minutes.

From the second experimental results, we find that our algorithm is able to find the real motifs from given gene sequences in little time. Our algorithm shows higher speed than other four motif finding methods, because an initial motif pattern is first extracted from comparing two sequences in the first stage of our algorithm. In addition, unlike Gibbs sampling and EM methods, our algorithm could avoid some extra time consuming computations, such as the calculations of likelihoods. According to this feature, we use the consensus string of the voting operation obtained from the result of last iteration as a new starting pattern to program, and continue doing voting until there is no further improvement. Experimental results show that if we set the number of iterations to be large enough, the program could give more accurate results in reasonable time. Besides, in order to detect unknown motifs in sequences, our program also provides several possible motifs existed in specific sequences, and the average mismatch numbers of motifs that is greatly lower than other four methods.

8. Future works

Compared with other tested motif finding methods, we could find that the voting algorithm has advantages in some aspects, but there are still some improvements could be done on this algorithm. As we know, though a set of sequences may have the consensus, but each motif in sequence may has mutations, and the length of each motif could also be different. So the two factors increase the difficulties in finding unknown motifs. In the future, we plan to improve the efficiency of voting

algorithm by studying other motif finding methods, such as MEME, a combination may be made between voting algorithm and MEME so that voting algorithm could have better performance in finding unknown motifs.

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